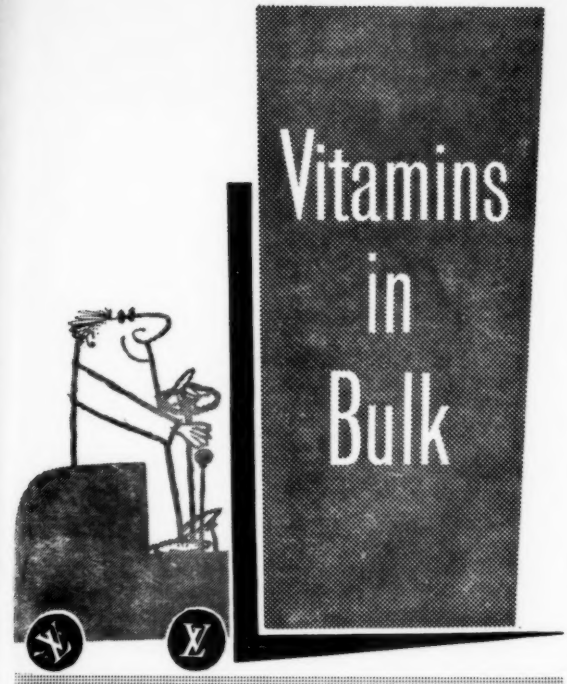

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Manufacturing Chemist

Editor: W. G. Norris

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The Packaging Buyer likes it
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Communist trade: the U.S. view

THE American chemical industry is clearly upset and perhaps alarmed by the sale by British manufacturers of plants and processes to Russia and her satellites. Why else should General Hull, president of the Manufacturing Chemists Association, devote most of his speech at the Association of British Chemical Manufacturers annual dinner to telling his large audience why his members won't trade with the communists? The arguments he put forward are those that I.C.I.'s chairman, Mr. S. P. Chambers, dealt with a few months ago in a speech at the English Speaking Union in London (see these notes August, p. 326).

General Hull said that under the new seven-year plan the Soviet chemical industry is supposed to expand 300% by 1965 and £9,000 million have been allocated for this expansion, plus £6,000 million for the petroleum industry, much of which will be for petrochemicals. These are immensely ambitious plans; as a yardstick General Hull pointed out that the entire assets of the U.S. chemical industry are worth £8,500 million. The Americans doubt strongly that the Russians can achieve their goals because of shortages of skilled men and of equipment. That is why Mr. Krushchev offered to buy 100 million dollars' worth of American chemical equipment and technology, an offer that was firmly turned down.

The Americans think that by selling plants and processes complete the Russians are enabled to avoid diverting efforts from their military programme. Admittedly they will eventually catch up with Western chemical technology, but the Americans see no reason why the West should barter away its present technological margins. They also fear that the Russians will give away process secrets to other communist countries, including China. So, apart from the straightforward military aspects of selling know-how to the Russians, there is the prospect that the whole of the communist bloc will eventually be able to compete with Western chemical exporters by exploiting processes bought from the West.

There is merit in these arguments and there will be sympathy with the Americans in the present state of the cold war. But General Hull did not effectively rebut the opposing arguments put forward by Mr. Chambers, which are undoubtedly supported by many British chemical industrialists. Can it be imagined that the Russians would allow the production of consumer goods to interfere with their military programme? The question of whether or not the Soviet chemical industry makes detergents or enriched uranium is not settled by the wishes of the consumers but by the Kremlin. As for the Russians giving away process secrets bought from the West to their satellites, we can be sure that the Kremlin would not permit this on a scale that would threaten their own economy. The Russians are careful to arrange these matters so as to leave themselves in control. Otherwise the Chinese, for instance, would be much stronger industrially than they now are.

The bogey of low-cost Russian exports driving the West from their markets is not a new factor for British exporters, who already have to face this competition from other countries, not least the United States. World trade looks very different from Washington than it does from London and British industry must continue to exercise its own judgment on the way it can best earn its living in the world.

Credit and cash

IN THE *Sunday Express* a few weeks ago, Mr. John Gordon compared the profits made from inventions with the rewards given to the inventors. Both examples he quotes come from the chemical industry. He alleges that last year the I.C.I. royalties on *Terylene* amounted to £800,000, but that the co-inventor, Mr. J. R. Whinfield, received a mere £600. And for his part in synthesising M. and B. 693, it is stated that Dr. M. A. Phillips received from his then employers, May and Baker, a single payment of £50. "How fair is fair in a money carve-up?" asks the angry Mr. Gordon.

Since the question of rewards to inventors is so rarely raised it seems that scientists in general are satisfied with the present system. This recognises that modern industrial discovery is hardly ever the work of a single, inspired genius. It is a product of team work to which everyone in an organisation contributes. In the drug industry, thousands of compounds must be made, tested and discarded for every successful drug produced. Who should get the credit (and the cash) for being the one to synthesise a successful drug? The shareholders who provide the facilities, the directors who authorise a particular programme of research, the director of research who plans and instructs, the dozens of chemists patiently toiling at the laborious process of elimination, the pharmacologists and pathologists who screen the compounds, the laboratory staff who do all the dogsbody work, the production and sales staff who make and market the drug? The answer, of course, is that they all deserve a share of the credit and the profits.

What sort of a research organisation could be run on the basis of payment by results? Would it not breed fear and jealousy and make vital co-operation impossible? Would it not result in waste and duplication and chemists working behind locked doors, fearful that colleagues might steal their secrets?

No research chemist in his senses could possibly prefer this system to the one whereby his salary and position are guaranteed for the whole of his working

life, irrespective of whether or not he produces a single profitable invention. Chance favours the trained mind, as Ehrlich once said, and everyone who knows anything about the frustration and disappointments of research knows that it is more often luck than genius that brings success.

Whether or not in the particular instances quoted the inventors were properly rewarded is not for us to judge. But it is tendentious and misleading to pretend that "big business" is immorally exploiting the work of individual scientists. What do our readers think?

Capsuling automated

In the last thirty years the history of the gelatin capsule has virtually been the history of Scherers. Robert Pauli Scherer, founder of the company, invented the rotary die machine in 1932 and production of flexible capsules started in Detroit, U.S.A., in 1933.

Now Scherers manufacture nearly 90% of all flexible capsules produced and the substances encapsulated include pharmaceuticals, vitamins, solvents, cosmetics, adhesives and polishes.

Their latest step forward is an automation process which we saw recently at their British headquarters at Slough. The machine which performs this is known as the integration capsulation unit, and unlike earlier machines, handles the capsule from the time it is produced in the rotary dies until the final drying stage.

Each unit comprises a capsulation machine similar in basic principle to the earlier types of rotary die capsulation machines, but to which has been added automatic transfer equipment which makes it possible for the operator to leave the machine unattended.

The gelatin and filling materials for the capsules are supplied to the machines in bulk tanks of approximately 50 gal. capacity and the material is automatically controlled by pneumatic valves to maintain the correct levels in the spreader boxes from which the gelatin ribbons are cast, and also to maintain the correct level in the small tank feeding the metering pump which injects the fill into the capsules.

After the capsules are formed in the rotary dies, they are transferred by a shaker chute to a belt conveyor which then transfers them intermittently to the first stage of a solvent washer. This first belt conveyor is arranged to keep the capsules separated before they go into the first wash basket. From this basket they are transferred to two further solvent washes and then to two draining stages. From this they pass through five heating stages with air blast and finally a cooling stage with room temperature air blast.

The capsules are then placed in drying tunnels for 12-14 hr., removed and finally inspected so that only perfect capsules are sent out. A final wash in large centrifuges completes the process before packing and distribution.

Anti-freeze—a cold war

The anti-freeze season opens with a bigger potential market than ever. There are some 5 million private cars on the road and sales are expected to exceed £4 million. Boots have set a cracking pace for their competitors by cutting their prices—1s. 6d. on a ½ gal. tin and *pro rata*. Their new price of 15s. is 4s. 8d. less than that of their nearest rivals, Holts, and over 10s. less than that of *Bluecol*, a brand that holds two-thirds of this rich little market.

Motorists may ponder hard on these price differences. Why, if anti-freeze consists of 90% ethylene glycol, should these discrepancies exist? Boots say boldly that the cost of inhibitors (they use triethanolamine phosphate and sodium mercaptobenzothiazole) should not make any significant difference on the price. Ethylene glycol in bulk costs about 14s. gal., complete with inhibitors. So even Boots' price of 29s. gal. leaves a good margin for repacking and distribution costs and profits. It is difficult to understand how higher, in some cases considerably higher, prices can be justified. Certainly the technical differences between the mixtures cannot account for it. Is it another case of charging what the market will bear?

Out of bounds

A great many people, including trade unionists, think trade union leaders should pay more attention to their members' jobs rather than waste time arguing whether or not Britain should possess nuclear arms. Ever since Ernest Bevin certain leaders of big unions have fancied their chances as world statesmen and seem to regard themselves way above the real job for which they are paid. We are moved to these remarks by some comments of Monsanto's chairman, Sir Miles Thomas, in a new paper, the *Weekly Post*. He crystallises the views of millions when he advises union bosses to bring their minds out of the orbit of the H-bomb, climb out of the political arena, and set about ensuring good wages and full employment for their members.

It has always puzzled us that a man whose sole experience of life has been in trade union affairs (how else would he rise to the top in his union?) should suddenly try to assume political skill, knowledge and authority. Our politicians have to submit themselves to the electorate before they become M.P.s, but the politically ambitious union chiefs try to dictate the policy of Britain without the slightest authority of the people. Their posturings would be less important if they did not wield authority in the Labour Party, the alternative government of Britain. It is to be hoped that the responsible leaders of the Parliamentary Labour Party will be able to put the union chiefs in their place.

Meanwhile employers might ponder on another comment from Sir Miles Thomas. Employers should keep striving for the confidence and loyalty of their workers; they must not surrender the task of direction and enlightenment to the trade unions.

Lac Sulphur

THE exploitation of the enormous deposits of sulphurous gas in the Pyrenees by the Société Nationale des Pétroles d'Aquitaine includes the production of sulphur at what is claimed to be the world's largest sulphur plant at Lacq. Thus the name Lacq Sulphur has been introduced into chemical commerce. To an older generation of chemists and pharmacists, this name meant something quite different, namely, Lac Sulphuris or Milk of Sulphur. Lac Sulphur had its heyday when it was a regular routine to dose children with brimstone and treacle. Lac Sulphur was a more refined preparation than the somewhat barbarous flowers of sulphur used in brimstone and treacle. The misleading term "flowers of sulphur" disguised the fact that it was usually crude sulphur which had been sublimed once in old-fashioned glass bumbelows. Lac Sulphur has a long history. Here is how it was made 230 years ago, according to Dr. John Quincy in his Pharmacopœia Officinalis and Extemporea:

"Take clean Salt of Tartar 1 lb, Flowers of Sulphur 6 oz, grind them well together in a Stone Mortar then further into a strong earthen Pan and add of Fountain Water 8 lb. Set this Mixture over some live coals and by degrees make it boil till the Liquor is very red, which will require three or four hours. Take it from the fire and before it is quite cold filter it, then drop into it distilled Vinegar which will cause the red Liquor to be muddy and a white Powder will precipitate. When the first Precipitation is fallen, drop in more Vinegar and so proceed till the Vinegar will not make the Liquor muddy any more. After this let all settle and by gentle Inclination pour off the Liquor, put Fountain Water to the magistery, stir it well about and let it settle, pour off as before and so proceed with six or eight Lotions till the Powder is insipid and free from Urinous taste."

The bitter end

WE HAVE tasted a new product which is six times more bitter than brucine and quassin and must thus qualify for the distinction of being the bitterest substance known. Finding this new substance, which is a synthetic chemical, has not been an academic exercise in organic chemistry, nor has it been done at the behest of brewers seeking to give a new character to their draught bitter. No, the chemical has no edible purpose whatever but, rather, is designed to make unpalatable that which might otherwise be consumed, namely ethyl alcohol and, perhaps, sub-standard vegetable oils that the unscrupulous might try to divert from their proper use in soap-making to food purposes.

Discoverers of the new substance are T. and H. Smith Ltd., of Edinburgh, whose qualifications for the exercise derive from their long acquaintance with brucine, which is present in nux vomica seeds from which, of course, strychnine is also extracted. There is a shortage of brucine, so Smiths have been screening bitter chemicals for two years. Not all are suitable for addition to alcohol, but eventually the new substance was synthesised. It is called *Bitrex*, but its chemical name is not disclosed.

The American authorities have approved the chemical as a denaturant for toilet ethyl alcohol. A quarter ounce of the white crystalline powder is sufficient to treat 100 gal. of ethyl alcohol; this is one-sixth of the quantity of other substances needed to produce the same effect. *Bitrex* is non-poisonous, non-corrosive and does not irritate the skin. It may have applications in the manufacture of agricultural products, insecticides, textiles, veterinary preparations and detergents. Since it is synthetic, its potency can be controlled and its supply assured. Although dearer than natural bitters it is more economical because of its far greater strength.

Computer at the chemists

ONE of the biggest problems of any large manufacturing concern with many branches to serve is that of warehouse distribution and stock control. To marshal the lines so effectively that even the most popular will not run out and even the most obscure are available at short notice is practically impossible by normal methods. But this ideal can be brought very much nearer by the use of electronic data processing. We witnessed this in operation recently at the central office of Boots in Nottingham where the company has installed the Emidec 1100 Data Processing System which is claimed to be the largest single commercial installation in Great Britain.

Basically the system works in the following manner. When an assistant in one of the 1,300 Boots branches needs to re-order stocks of certain categories of goods in high demand, all that she needs to do is to make a few pencil strokes at precise points on a printed card. From this card her order will be automatically converted into punched card or tape form and then read into the Emidec.

To speed up the process of assembling the order, the computer will automatically sort out the items into the sequence in which they are to be picked up in the warehouse. It will make the necessary adjustments to stock totals and will print out an extended invoice for dispatch with the goods. Items out of stock will be "remembered" and supplied automatically as soon as they come through.

The whole task of merchandise accounting that the machine performs includes handling of routine, supplementary and special orders from branches; preparation of order-assembly instructions in warehouse bin sequence; automatic printing of extended and totalled invoices; perpetual inventory of warehouse stock; accounting for supplies delivered to branches; out-of-stock and critical-stock warnings to buyers; statistical studies of demand for buyers and for production planning; ability to compute purchase tax liability; and preparation of profitability statements.

The next step in this modernisation at Boots will

be to automate the warehouses and connect them up directly or indirectly to the computer so that the machine actually does the picking from gravity chutes on to a conveyor belt as it reads the order.

It is obvious that the savings made in speeding up routine work will certainly balance the expense of such an installation, but the real value is to be found in the new thinking that it makes possible.

Come to the show

CHEMISTS are interested in corrosion both as an industrial problem and as a fascinating scientific study.

Paints, plastics, resistant metals, inhibitors, metal finishing, dip coatings, cathodic protection and many other anti-corrosion weapons are the products of chemical science and technology. So with this double interest for chemists the Corrosion and Metal Finishing Exhibition at Olympia this month is bound to be a great attraction for our readers. The organisers—our associated journal *Corrosion Technology*—have excelled all their previous efforts and arranged an exhibition containing over 120 stands and occupying over 50,000 sq. ft. We strongly urge our readers to go to the exhibition in force. There has been a wide distribution of tickets. If you haven't got one you can get in free by producing your professional card. And don't forget the technical meetings and film shows that are innovations this year.

Pooling research resources

THE RAPID evolution of science and technology is continually exposing gaps in resources and effort. In the opinion of the Advisory Council on Scientific Policy, chief advisers of the Minister of Science, these "growing points" are found most frequently in areas lying between the traditional disciplines and involve the participation of several of them. The answer is not always to be found in the creation of new university departments and new disciplines. The Council think that universities should rather encourage the effective interaction of traditional skills. They should be more ready to introduce into existing departments new developments which lie in part outside the scope of the traditional disciplines for which they were created. The development of Colleges of Advanced Technology and the expansion of smaller universities present golden opportunities to promote studies in fields where there is little or no tradition of research and its application and where there is little interaction between the universities and the industries which are the customers for the resulting technological skills. New universities will have the opportunity to establish departments covering the applied sciences in a less orthodox pattern. And the time is ripe for greater co-operation in the use of expensive facilities between the universities, the C.A.T.s and government establishments.

Collaboration to make the best use of limited scientific resources is the advice that permeates the Council's report for 1959-60. Britain spent £480 million on research and development in 1958-59, a sum equal to 2·35% of the gross national product. America spent 2·74% of its G.N.P. on research and development in the same period but this amounted to £3,971 million, more than eight times Britain's expenditure. So to make the best use of what we have, not only should universities collaborate; the Council advises industry to do likewise. Fragmentation of research is wasteful and even international collaboration should be considered to help Britain and like-minded countries to produce scientific advances comparable with those made by Russia and the United States. In a free and competitive economy, collaboration sets a tremendous challenge.

Cheque mate

WE ARE told that London is once more the financial centre of the world and we are sure that our bankers would like to think that their names ring into the four corners. But what can happen when an English cheque arrives at a distant destination has been described to us most movingly by a contributor in the United States.

"A real honest-to-goodness cheque from Merrie England creates quite a little excitement when we take it proudly into a bank here in back-country Alabama. First, the teller looks at me suspiciously. Then he notes that the cheque on Barclay's Bank is not long and narrow like ours but more nearly square in configuration. At that point he feels pretty sure that I've forged the thing myself. Then he tosses the cheque in the air and lets it flutter down on his marble counter. There is no familiar bell-like tone as one hears when he flips a silver half-dollar and listens for the ringing sound that stamps it as genuine. The teller is about to ring for the armed, uniformed guard at the door when he remembers the 'bite' test, used to distinguish silver from soft-metal counterfeit coins. So he nibbles at a corner of Barclay's cheque, doesn't like the taste, and is just beckoning the guard when I say, 'If you'll accept the cheque on probation, subject to examination, and give me a receipt—?' So, he puts the cheque through for collection (which doesn't obligate the bank in any way), and after the cheque has been sent to New York, to Washington, to the White House, back to New York, then to Tuscaloosa, and finally back to Barclay's Bank in London, I get the money from which has been deducted 'two bits' (twenty-five cents), which seems to be the Federal amusement tax. When the government has collected enough two bits it is able to buy gasoline to send another plane over Russia for the Bolsheviks to shoot down.

"Please understand: I'm perfectly happy about Barclay's cheques. It's the best system of handling the funds. Anyway, two bits won't buy a loaf of bread here and the bread isn't anywhere nearly as good as the loaf that ten cents used to buy in 1918. . . ."

Calf severely affected by parasitic bronchitis standing in the typical " air-hunger " position.

The World's First Parasitic Vaccine

By N. C. Craig Sharp,* B.V.M.S., M.R.C.V.S.

Parasitic bronchitis (husk) is a severe disease of cattle which depletes herds and causes serious losses to farmers. There are now two methods of countering husk: direct attack on the parasitic worms with drugs (diethyl carbamazine and cyanacethydrazide) and prophylaxis with a new oral vaccine, the first of its kind in the world. Here the author describes the development and manufacture of the vaccine by irradiating larvæ with X-rays, and discusses the possibility of producing other parasitic vaccines, including the culturing of enzyme-producing tissues.

BECAUSE of their size, the larger parasitic worms were among the first agents recognised as being capable of causing disease, over 3,500 years ago. Today, in many parts of the world, parasitism represents a formidable problem—for example, over 1,000 million people are estimated to be infected with the two most prevalent human parasites—the hookworm and the common roundworm. The problem is one mainly of underdeveloped countries, but the initial steps towards a higher living standard in the form of irrigation projects may lead to a worsening of the situation, as actually happened in the Aswan province of Egypt, the Belgian Congo and in Southern Rhodesia, where incidences of the disease bilharziasis (caused by a small flatworm) rose to between 10 and 40 times the previous levels after the establishment or extension of such irrigation schemes,[1] due to the resulting vast increase in the numbers of water snails which harbour the intermediate stage of this trematode.

* Dept. of Hospital Pathology, University of Glasgow, Veterinary School.

Similarly, in animals, advances in agrarian techniques, leading to greatly increased concentrations of livestock on pastures, have immensely facilitated the spread of parasitism, thus reducing production of milk, meat and wool and causing serious financial loss which, in America, has been estimated at $227,000,000 per annum.[2]

However, there is a brighter side to the picture; many highly successful anthelmintic drugs have been developed and, of course, more are at the experimental stage as readers of MANUFACTURING CHEMIST will no doubt be aware, having read Mackie's most interesting article on the chemist's approach to helminthiasis.[3] Recently, too, a breakthrough was made on a different approach, that of actually preventing a parasitic disease by vaccination; this advance was made by a team of scientists at Glasgow University Veterinary School. It is with this new development that this article is concerned.

Some infectious diseases elicit a strong and lasting immunity if the human or animal recovers from them, while others confer little or no protection—the common cold, for instance. Parasites are no different in this respect—some confer excellent immunity on recovery from the infection, while others seem unable to evoke such a response naturally.

Principles of vaccination

Vaccines, both living and non-living, have been widely used against bacterial and viral infections, but until recently no such artificial aid to immunity was available in the parasitic field. The principle behind vaccination is that the introduction of foreign protein into the body elicits the formation of specific antibodies which attach themselves to it and, if it is a microbe, they either kill it or inhibit its multiplication, and lay it open to further attack by the scavenging cells of the body. Immunity to parasites occurs along these same fundamental lines, although some helminths by nature of their position in the body—*e.g.* in the lumen of the intestine—have very little opportunity to contact any site

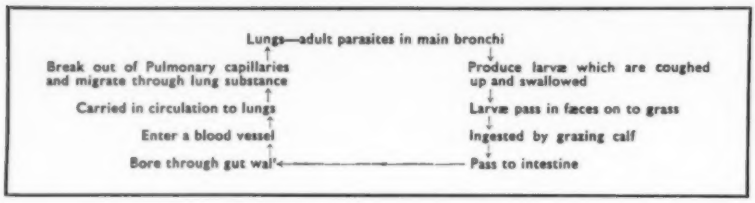
Lungs—adult parasites in main bronchi
Break out of Pulmonary capillaries and migrate through lung substance
Produce larvæ which are coughed up and swallowed
Carried in circulation to lungs
Larvæ pass in faces on to grass
Enter a blood vessel
Ingested by grazing calf
Bore through gut wall
Pass to intestine

Fig. 1. Life cycle of husk parasite.

of antibody formation and so may not trigger off an immune response on the part of the host.

The husk parasite

The parasite on which our fundamental work was done was *Dictyocaulus viviparus*, the causal agent of parasitic bronchitis (husk) in cattle, which is one of the major disease problems of the dairy industry in this country. The life cycle of this parasite is shown in Fig. 1.

The definitive site of the worm is in the main bronchi, and harmful effects caused by it are confined solely to the lungs; pathologically, these effects are very complex,[4] but the basic lesion is that of intense reaction by the lung (*i.e.* pneumonia) to the presence of the invading larvæ as they migrate from the small pulmonary blood vessels through the lung tissue to the bronchi (where they then start their main growth period). It is worthy of mention that this is one parasite against which a drug effective only against the adult form would be of comparatively little use, as the main damage occurs en route.

One big factor in our favour in our attempt to approach this disease from an immunological viewpoint was the knowledge that animals which did recover from an attack of husk were generally fairly resistant to further assault.[5] We tested this experimentally by comparing a group of such recovered calves to a group of normal calves of similar age, by administering to both groups a number of infective larvæ known to cause the disease in a severe form. The result gave ample confirmation to the fact that strong immunity did exist in this disease.

A further stage was to produce resistance artificially in calves through giving them known numbers of larvæ, and by challenging the animals with normally fatal doses we found that a high degree of resistance to subsequent re-infection was obtained and that this acquired immunity could result from either a single sub-lethal dose of larvæ, or from a series of repeated doses of small numbers of larvæ.[6]

The next step in the immunological experiments was to see if the immunity conferred by an infection with *D. viviparus* could be passively transferred to a susceptible animal.[7] A number of recovered field cases of the disease were challenged with serially increased doses of the larvæ. Blood serum was collected about a month after the final dosing and a globulin preparation was separated by sodium sulphate fractionation.

A group of young susceptible calves was injected intraperitoneally with the globulin solution in three divided doses, and was then challenged together with an equal number of controls, with 4,000 infective lungworm larvæ. Thirty days later both groups were killed and the numbers of worms in their lungs counted, as follows:

Immunised group—mean No. of worms per calf..	37
Control group—mean No. of worms per calf..	786

Two basic factors had now been established: (1) Resistance to the disease could be produced by controlled artificial infection. (2) This resistance could be passively transferred.

Active immunisation

Thus encouraged, we set about investigating methods of protecting calves by active immunisation—*i.e.* by stimulating the calves to form their own antibodies without, of course, producing the disease.

The first method tried was to collect adult worms from the lungs of experimentally infected calves immediately after slaughter. The parasites were suitably freeze-dried, emulsified with Freunds adjuvant and injected intramuscularly. Two extensive experiments were carried out,[8] involving 112 calves in various groups covering permutations of both vaccination and challenge schedules. All vaccinated groups showed a statistically significant reduction in "take" as compared to the appropriate controls. However, although the principle of active immunisation was established for the disease, the immunity was not of a very high order, and the method of vaccination employed was far too expensive for field use.

Evidence has been accruing in recent years that the stimulation of protective antibodies in the case of helminth diseases is greatest when living, actively metabolising worms

Lungs from a severely infected calf with heavy infestation of adult *D. viviparus* in the (opened) main bronchi.

are present — in fact, several workers [9,10] have shown that immunogenic potency lies in the actual secretions and excretions of the worms rather than their body material.

What we wanted therefore was a method of attenuating the larvæ so that they would remain alive and metabolising in the host tissue, preferably without reaching the lungs at all, for long enough to stimulate the antibody-forming mechanisms to lay down the "templates" for synthesis of the appropriate globulin (Fig. 2).

Attenuation with ionising radiations

After considering several possible methods, we decided to experiment with ionising radiations from an X-ray source as these had previously been shown to affect helminths.[11,12,13] Stage one of this project involved our standardising the roentgen dosage of X-rays administered to the larvæ. A preliminary trial gave an indication of the range required; within this we covered from 20,000 to 60,000 R. for our main trial, the group mean results of which are listed in Table 1.

Table 1. Quantity of irradiation necessary to achieve inactivation

X-ray dose to larvæ (Roentgens)	*Larval dose to calf*	*Group mean No. of worms in lungs at day 35*
20,000	4,000	4·2±3·5
40,000	4,000	2·0±1·7
60,000	4,000	0
Control	4,000	906±373

The calves were given 4,000 irradiated or normal larvæ according to their group and were killed 35 days later to find out how much inactivation was achieved at each level. From the preliminary trial it had been apparent that irradiation at less than 20,000 R. did not produce sufficient alteration of the larvæ, as our "vaccine" below this roentgen level produced clinical disease. It

3rd stage infective larva of *D. viviparus*.

was obvious that all three higher levels chosen gave very considerable inactivation compared to the controls.

Three further groups of calves were given the same numbers of larvæ irradiated at the same three levels. These, together with a fresh control group, were then challenged with 4,000 fully infective normal larvæ 50 days later and all were killed after a further 35 days. Table 2 lists these results.

Compared to the fully susceptible controls who harboured a mean of approximately 1,200 worms, the two lower roentgen groups showed an excellent measure of protection. 60,000 roentgens obviously was "over the top"—the larvæ here were possibly too inactive to even penetrate the bowel wall and, consequently, failed to reach a site where

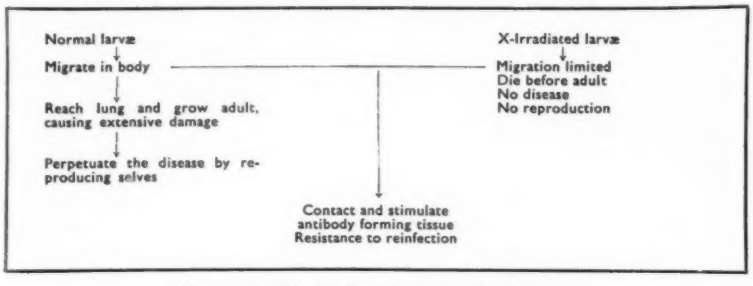

Fig. 2. Antibody forming mechanisms.

Table 2. Degree of immunity produced at each level of irradiation

Vaccination		*Challenge*	
Larval dose	*X-ray dose (Roentgens)*	*Larval dose*	*Resulting No. of worms in lungs*
4,000	20,000	4,000 normal larvæ	15·6±16·7
4,000	40,000	4,000 normal larvæ	13·6±18
4,000	60,000	4,000 normal larvæ	919·8±619
—	—	4,000 normal larvæ	1188·4±375

they could exert an effective antigenic stimulus. On the basis of these results, we chose 40,000 roentgens as our irradiation dose for future experiments, keeping such variables as X-ray filtration, kilovoltage, filament amperage, irradiation rate, backscatter, etc., as constant as possible. Having settled on the irradiation level, we had to standardise the number of larvæ in each vaccine dose. Too few would not provide an adequate stimulus for protection, too many would be merely wasteful.

Furthermore, as many vaccinating procedures involve two or more injections, we felt it necessary both to compare single and double vaccination with different larval doses,[14] and to test the resulting immunity with a much higher challenge—comparable to that which will produce the severe disease in the field. The experimental design and result is shown in Table 3.

Table 3. Design of double and single vaccine experiment and group mean lungworm burdens

All at 40,000 Roentgens

1st Vaccination No. of larvæ	*2nd Vaccination No. of larvæ*	*No. of larvæ in challenge*	*Worm burden in lungs*
1,000	1,000	10,000	0
1,000	2,000	10,000	0
1,000	4,000	10,000	0
1,000	—	10,000	820
—	—	10,000	1,020

The high challenge dose in this experiment did in actual fact swamp the single vaccination group, although the double 1,000 calves were as resistant as the other double dose groups.

Field trial results

Immediately prior to this experiment we had set up a small-scale field trial involving 30 calves,[15] only half being vaccinated, which were turned on to a 3-acre paddock heavily infested with lung-worm larvæ. Ten weeks later only 17% of the non-vaccinates were alive, com-

pared to 80% of those receiving irradiated larval vaccine, which is administered orally.

The next stage was to carry out a field trial on a very much larger scale; the 1957 trial using single vaccination with 1,000 larvæ involved 1,088 calves on 40 farms; the 1958 trial, in which double vaccination was applied, comprised over 8,000 calves on 206 farms.

Such field trials must, of course, have a considerable element of scientific uncertainty, due to the large number of variables pertaining on nearly 250 farms. Nevertheless, two facts of great importance emerged:

1. The vaccine was safe to use, and no undesirable properties showed up.
2. The incidence of husk was extremely low in all our vaccinated calves—much lower than other farms in the same area, which gave reason to believe that the vaccine was indeed proving efficacious.

Experimental production

As done in Glasgow, this involves the following:

(1) Infecting "culture" calves. Three-month-old parasite-free calves are dosed with 4,000 normal *D. viviparus* larvæ. Twenty-five days later, the next generation of larvæ appear in the fæces.

(2) Culturing larvæ. Larval-rich fæces, collected from the above calves, are layered in 100 g. portions into 8 oz. pomades, which are placed in a cool, dark, humid atmosphere for eight days to ensure that the first stage larvæ reach the infective third stage.

(3) Harvesting larvæ. Done by a simple washing procedure, the end result being a beaker of brown water containing larvæ. Coarse debris is removed by sieving.

(4) Counting larvæ. Done by a multiple sampling technique. Ten or twenty 0·1 ml. samples are pipetted on to glass slides; the larvæ are counted under a microscope.

(5) Irradiation. Carried out at a constant volume of 10 ml. for X-ray calibration purposes; the three or four litres of original solution are concentrated by sedimentation and centrifugation to this volume, which is transferred to a perspex dish placed at a specific distance from the X-ray tube. The machine is run for the appropriate time, which amounts to several hours.

Irradiation set-up. 500,000 lungworm larvæ in perspex container, on base of pressed wood.

(6) Preparation of doses. The original 10 ml. are reconstituted to a convenient volume and carefully recounted. Doses of 1,000 larvæ in approximately 25 ml. water are put into suitable bottles.

(7) Administration. The dose is given orally to each calf.

(8) Storage. Apart from vaccine longevity trials, we do not store any vaccine we make.

Process scale-up

The next logical step was to scale-up the process to the point of commercial production and the firm of Allen and Hanburys Ltd. undertook to do this; they had in fact carried out a preliminary production run in supplying all the vaccine we used in the 1958 field trial.

For various reasons, the scaling-up process proved a formidable—at times seemingly insoluble—task. We had only kept half-a-dozen infected calves at any one time; we had collected the fæces manually and cultured them in glass jars in enamel buckets and we irradiated comparatively small numbers of larvæ each time. Our doses were measured out by pipette and administered the same day.

Poynter and Jones[16] indicate some of the major difficulties involved on the commercial side of lungworm vaccine production when they state, "It is sufficient to say that the maintenance of a constant population of calves infected and managed in such a way as to produce an adequate output of larvæ without death, coupled with the extraction from the fæces of third stage larvæ, has proved to be a considerable undertaking. The final production of these larvæ, free of fæcal debris, and their subsequent X-irradiation and vialling, together with all the essential control and safety testing procedures, culminating in a final product with a limited shelf life, has also presented many difficulties."

While on the subject of commerce, it is perhaps pertinent to reiterate the point put forward by Mackie[3] that a chemical answer to the helminth problem would provide an extremely valuable export, as it already seems that this biological "answer" will prove important in a similar context; much interest has in fact been aroused all over the world and some countries are already planning to utilise the technique under licence.

Sheep nematodes

Our work did not, of course, stop at this stage; we have in fact turned our attention towards several other parasites. As was mentioned above, *Dictyocaulus viviparus* migrates extensively through the body and would appear to have an excellent opportunity of stimulating immune mechanisms. We were very interested to see if a parasite with a minimal migratory cycle, and resulting minimal chance of antibody stimulation, could in fact be made to yield a serviceable immunity.

Two bowel parasites of sheep were selected for this purpose, *Hæmonchus contortus*[17] (a stomach worm) and *Trichostrongylus colubriformis* (an intestinal worm), and a series of experiments were carried out separately on them both. We started as before, by finding the best

irradiation level, then the number of larvæ per dose, then whether double dosing was more effective—and in general followed the sequence outlined above for the lungworm.

Although we are still at the experimental stage with these sheep nematodes, the results so far are promising, as indeed are the findings from some of the half-dozen other parasites with which we are working, especially the dog hookworm, *Uncinaria stenocephala*.[18] If all continues to go well, vaccines against several parasitic diseases may follow. Quite a large proportion of our thought and work at present is devoted to studying where the sites of antibody formation actually occur—especially in husk—and what the exact cellular manifestations of this immunity are.

Enzyme production

Equipped with detailed information of this nature, we may then be in a position to improve on our vaccinating procedures. Although *Dictol*, to give the product its trade name, is the world's first parasitic vaccine, the technique of its production is very laborious. Great stress is being laid on the importance of the so-called metabolic products of helminths in immunity and an explanation favoured by many workers, including Chandler,[19] is that such immunity has an anti-enzyme basis. If enzymes themselves are the real antigens—might it not be possible to culture artificially the appropriate enzyme-producing tissues and make parasitic vaccines in this way—eliminating irradiation altogether?

We have established that vaccination against parasitic disease has become a practical fact, and my own hope is that the resurgence of interest in parasitic immunity which has occurred during the last decade, will lead to many more such practical facts.

Acknowledgement: I would like to thank Miss Margaret J. Cockburn for typing the manuscript.

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VACCINE EQUIPMENT

The most important ingredient for a foot-and-mouth disease vaccine is the virus. This was formerly obtained from material originating from artificially infected cattle. During the last ten years Dr. H. S. Frenkel, Director of the State Veterinary Research Institute (Netherlands), has succeeded in cultivating the virus in large quantities in living cattle tissue. The virus required for the preparation of vaccine for the annual vaccination of about 3 million head of cattle in the Netherlands has been produced in this manner for several years. Using Dr. Frenkel's directions, Ensink N.V., of Hilversum, have built an apparatus in which this virus can be cultivated. It consists of a constant-temperature water bath which can hold five culture vessels. A central driving gear ensures agitation in the vessels. The charge per vessel is about 30 litres, hence the total capacity of the apparatus is 150 litres. The continuous oxygen flow is regulated for each vessel separately.

To facilitate research work it is possible to control temperature, stirring speed and stroke of the stirring mechanism in one of the vessels, irrespective of the value of these variables for the other vessels. The apparatus is so constructed that it can be installed in a laboratory without special provisions.

Honey in Pharmaceuticals

LITTLE information has ever been published concerning honey as a vehicle for medicinal preparations.

Recently, a two-year research programme into this problem was instituted at the Philadelphia College of Pharmacy and Science by the U.S. Department of Agriculture, by Drs. N. Rubin, A. R. Gennaro, C. N. Sideri and A. Osol.

According to their findings, honey improves the palatability of many medicines with its pleasant, natural flavour. Furthermore, medicines in honey preparations settle slowly and can be resuspended by moderate shaking. For tonics, cough medicines, and some vitamins, honey solutions are entirely stable. For other vitamins, stability is limited to two or three weeks, and for aspirin to several days.

Research showed that an iron tonic, ferrous sulphate syrup, usually made in sugar syrup flavoured with peppermint, can be made with honey as the sole flavouring agent. It is stable, exceptionally palatable, and free of the astringent after-taste characterised by most preparations containing iron.

Sulpha drugs, such as sulphadiazine, sulphamerazine and sulphamethazine, are usually marketed in the form of liquid suspensions. Experimental preparations of these drugs in suspensions composed mostly of honey were preferred by taste panels over other commercially available preparations. They were also completely stable, slow to settle, and easily re-suspended.

Cough preparations containing anti-histaminic agents and codeine, and also a terpin hyrate elixir that is widely used as a cough remedy, were made in palatable and stable forms using honey as the vehicle.

Vitamin B_2 (riboflavin) is especially stable in honey solutions. Vitamin B_1 (thiamine) alone is not as stable in honey solutions as in other vehicles, but it is sufficiently stable if vitamin B_2 also is present in the preparation. Vitamin B_{12} (cyanocobalamin) and vitamin C (ascorbic acid) are not stable in honey, but would be suitable for immediate use.

The research also showed that medicinal products prepared with honey and containing water can be preserved from microbiological degradation by the addition of sorbic acid to the honey solutions.

The Tetracyclines

By M. L. Burstall, D.PHIL.

Although the tetracycline antibiotics, exemplified by Aureomycin and Terramycin, are well established in medicine, they still offer commercially attractive research possibilities because from them may be produced a wide range of biologically active analogues and derivatives which may prove active against pathogens resistant to the parent compounds. These possibilities lend particular importance to this comprehensive review of the chemistry, manufacture and pharmacology of the tetracyclines. As a former worker in this field Dr. Burstall is well qualified to write this review.

THE tetracyclines are a group of broad-spectrum antibiotics, active against both Gram-positive and Gram-negative bacteria, which are based on the structure (I) (R_1=H or Cl; R_2=H or CH_3; R_3=H or OH):

Since the discovery of the first tetracyclines, oxytetracycline (Terramycin) (I; R_1=H, R_2=CH_3, R_3=OH) and chlortetracycline (Aureomycin) (I; R_1=Cl, R_2=CH_3, R_3=H), they have been the subject of a volume of research unusual even in this highly interesting and profitable field. Interest was initially aroused by their combination of a wide antibacterial spectrum with an absence of serious side-effects, and by their bizarre structure, which presents the organic chemist with a new problem in synthesis. It has subsequently been stimulated by the discovery that, unlike most antibiotics, their structure may be extensively modified without destroying their antibacterial properties. Indeed it may be said that none of the older antibiotics, and very few of the newer ones, present more features of scientific and commercial interest than do the tetracyclines.

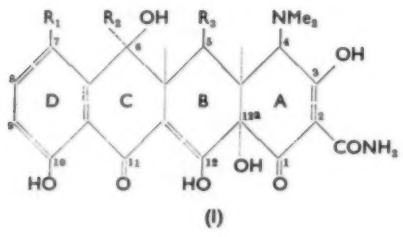
The tetracyclines are obtained commercially as byproducts of the metabolism of various *Streptomyces* species.[1] The elegant tracer studies of Snell[2,3] and of Birch[3] have revealed the route by which they are formed. It appears that glutamate is a unique, and probably direct, precursor of the C_2-C_{4a} part of ring A and of the 2-carboxyl and 4-amino groups. The rest of the naphthacene ring system is built up by the head-to-tail condensation of acetate residues; larger molecules, such as pentoses, hexoses or shikimic acid, which are known in other cases to be precursors of aromatic and hydroaromatic ring systems, are not involved[4] as intermediates. This mechanism is similar to that proposed for the biosynthesis of the hydroxyanthraquinones[5] and of the recently discovered naphthacene antibiotics aklivin[6] and ε-pyrromycin.[7]

The N-methyl and C_6-methyl groups are subsequently introduced by direct biological methylation (II). The chlorine atom of chlortetracycline is also very probably introduced after the ring system is formed. It is significant that cultures which normally produce chlortetracycline will produce[8] tetracycline (I; R_1=R_3=H, R_2=CH_3) itself if grown in a chloride-free medium, and a bromotetracycline[9] (I; R_1=Br, R_2=CH_3, R_3=H) in a medium containing bromide and no chloride.

Commercial production

These reactions are realised in practice by growing the *Streptomyces* species in a well-stirred and aerated sterile aqueous medium containing biological carbon and nitrogen sources, calcium carbonate, ammonium and magnesium salts, and small amounts of the trace elements required by the organism. The carbon source may be glycerol,[4] fatty acids and their derivatives, glucose, sucrose, corn sugar, molasses, starch, or other carbohydrates;[10] it is reported[11] that lactose promotes sporulation and sucrose fermentation. The nitrogen source may be ammonium salts, synthetic amino-acid mixtures, casein digest, yeast, or more commonly corn-steep liquor, soya-bean flour or cottonseed endosperm flour;[4,12] it is apparently advantageous to use more than one of these sources.

In a typical process[13] 20,000 gal. of a mixture containing 3% sucrose, 3% corn-steep liquor, 0·9% calcium carbonate, 0·33% ammonium sulphate, 0·2% magnesium chloride, and 0·005-0·0005% of ferrous, manganous, zinc and cobaltous salts was inoculated with a *Streptomyces aureofaciens* strain and then stirred and aerated for 62 hr. at 27° and a *p*H of 4-5 to give a mash containing 2,500 γ of chlorotetracycline per ml. and 742 γ of vitamin B_{12} per litre. The formation of tetracycline rather than chlortetracycline under these conditions is possible if a completely chloride-free medium is used, or, more conveniently, if small amounts of bromide ion[14] or 2-mercaptobenzthiazole[15] or related compounds are added to the fermentation mixture.



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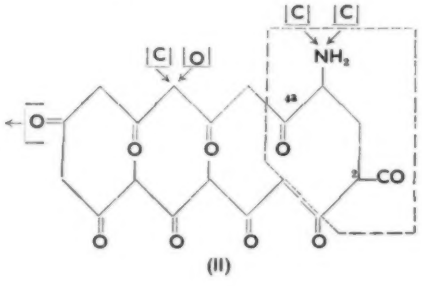

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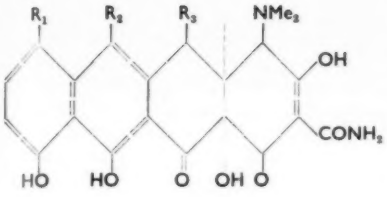

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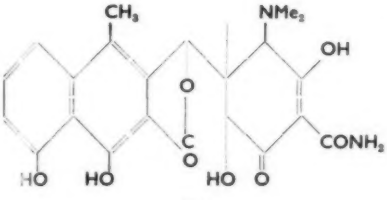

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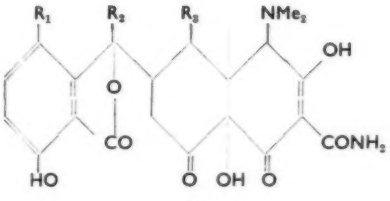


(VI)

The extraction of the tetracyclines from the fermentation mash has been much investigated. In the most favoured method[16] the mash is acidified to *p*H 2-3 and filtered to give a clear broth from which the tetracycline is precipitated at *p*H 8·5-9·5 in the presence of divalent metal cations as the salt with a cationic surfactant such as *Arquad C*. The salt may either be collected or extracted into butanol or ethyl acetate; subsequent treatment with mineral acids liberates the tetracycline. A plant operating such a process has been described.[17] Alternatively the tetracycline may be precipitated from the broth at *p*H 8-10 as the highly insoluble calcium or preferably mixed barium-magnesium salt,[18] or at *p*H 1-1·5 as the chelate compound with ferric iron.[19]

The crude tetracyclines may be purified *via* their salts,[20] or by chromatography on ion-exchange resins or cellulose phosphate.[21]

Properties

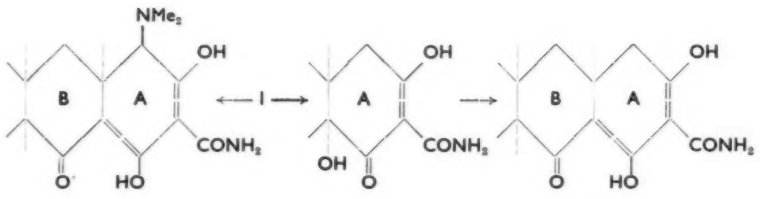
The tetracyclines are pale yellow solids, fairly stable to heat—thus oxytetracycline loses only 20% of its activity when heated *in vacuo* for 40 hr. at 105°—and to storage in the dark when dry.[22] They are amphoteric in character—tetracycline hydrochloride has pK_a values of 3·3 (basic) and 7·8 and 9·5 (acidic)[23]—and form stable derivatives with both acids and bases. The numerous salts with acids are in general[24] nicely crystalline solids which are stable to storage and rather sparingly soluble in water; the complex sodium hexametaphosphate is of importance[25] because of its rapid absorption into the body from aqueous media. The tetracyclines all form red or yellow chelate compounds with many metal ions.

These may have a tetracycline : metal ratio of either 1 : 1 or 2 : 1. Their stability varies with the metal used in the order:

$$Fe^{3} > Al^{3} > Cu^{2} > Fe^{2} > Co^{2} > Mn^{2} > Mg^{2}$$

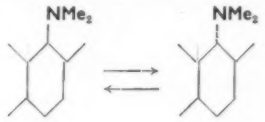
the nature of the tetracycline being of little importance.[26] A comparison[27] of the effect of metal ions on the absorption spectrum of oxytetracycline with the effect of such ions on the spectra of various model compounds suggests strongly that the ligand group is the enolised β-diketone system lying between C_{11} and C_{12}. The possible biological significance of these compounds is discussed below.

The stability of aqueous solutions of the tetracyclines depends both on the structure of the tetracycline and on the *p*H of the solution. In strongly acid solutions (*p*H>1) all the tetracyclines are smoothly dehydrated[28] to the biologically active anhydrotetracyclines (III) (R_1 = H or Cl; R_2 = H or CH_3; R_3 = H or OH).



(IX) (VII) (VIII)

In mildly acid (*p*H 3-6) solutions both the tetracyclines and the anhydrotetracyclines undergo a slow, reversible, epimerisation about C_4 to give [29] the corresponding *epi*-tetracyclines (*Quadrimycins*) (V), which are biologically much less active than the parent tetracyclines.



(I) (V)

Finally, in mildly alkaline (*p*H8) solutions the C-ring of the tetracyclines is opened to yield the biologically inactive *iso*tetracyclines (VI). This reaction is markedly accelerated by the presence of substituents at C_7; thus in aqueous bicarbonate solution the half-life of chlortetracycline is 3 hr,[30] while that of tetracycline itself under the same conditions is 30 hr.

Anhydrotetracycline (III; R_1 = R_3 = H, R_2 = CH_3) and anhydrochlortetracycline (III; R_1 = Cl; R_2 = CH_3; R_3 = H) are both very stable to both acids and bases, but anhydrooxytetracycline (III; R_1 = H; R_2 = CH_3, R_3 = OH) is rapidly converted by either to the inactive *apo*-compound (IV), which then undergoes further transformations. It is probable that the B-ring is opened to give (IV) by a direct attack of the 5-hydroxyl group on the C_{12} carbonyl group.

This may be the reaction by which the tetracyclines are destroyed in the body. It is obvious that they are stabilised towards both acids and bases by the absence of the 5-hydroxyl and 7-chloro groups.

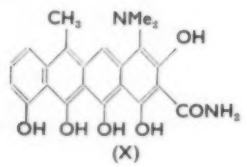
Modified structures

The study of tetracyclines of modified structure is of great value in the elucidation of the connection between structure and biological activity in this series. Three general methods have been used in the preparation of such compounds (for the sake of convenience compounds known to have some antibacterial properties are italicised):

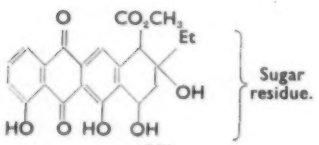
1. The selective reduction of the tetracyclines. It has been found that reduction with metals affects only the A-ring. Thus, reduction of tetracycline with zinc and acetic acid yields successively *4-dedimethylamino-*(VII) and *4-dedimethylamino-12a-deoxy-*(VIII) *tetracyclines*,[28] while reduction with zinc

and ammonium hydroxide yields *12a-deoxytetracycline* (IX).[31]

It is worth noting that compounds which lack the 12a-hydroxyl group are enolised in a different way to the tetracyclines, and, unlike the latter, are readily dehydrated by acids to derivatives of the wholly aromatic terrarubein (X).[28] This last compound may, by analogy with aklivin (XI),[6] have antibacterial properties.

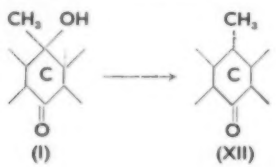


(X)



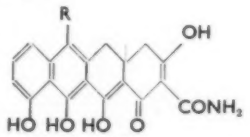
(XI)

In contrast to this behaviour, the catalytic reduction of the tetracyclines affects only the C and D rings. The reduction of neutral solutions of the 7-halotetracyclines over palladium merely removes the halogen atom; this reaction is exploited in the manufacture of tetracycline from chlortetracycline.[32] In acid solutions, however, the tetracyclines are smoothly reduced to the *6-deoxytetracyclines* (XII).[33] These compounds are readily nitrated and brominated to give 7- and 9-substituted derivatives, unlike the parent tetracyclines, which are preferentially dehydrated to the corresponding anhydrotetracyclines (III) under the conditions used.[34]

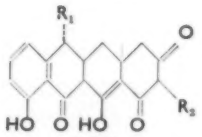


(I) (XII)

2. The total synthesis of tetracycline-like compounds. This is at once a spectacular and a time-consuming approach, and, as is well known, success in such endeavours is often attended by agreeable consequences for the lucky chemist; it is therefore hardly surprising to find that the synthesis of tetracyclines has been studied by American, British, German, Russian, Chinese and Japanese workers. The most successful approaches to have appeared so far start from a suitably substituted benzene derivative, which includes what is eventually the D-ring of the tetracycline, to which the C, B, and A rings are successively added by homologation and cyclisation. This route is conveniently illustrated by Muxfeldt's synthesis of the tetracyclines (XIII; $R = CH_3$)[35] and (XIV; $R_1 = CH_3$, $R_2 = H$).[36]



(XIII)



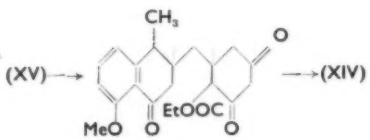
(XIV)

The key intermediate in both cases is the tetralone (XV), which was prepared in 39% yield from *m*-methoxyacetophenone as shown below.

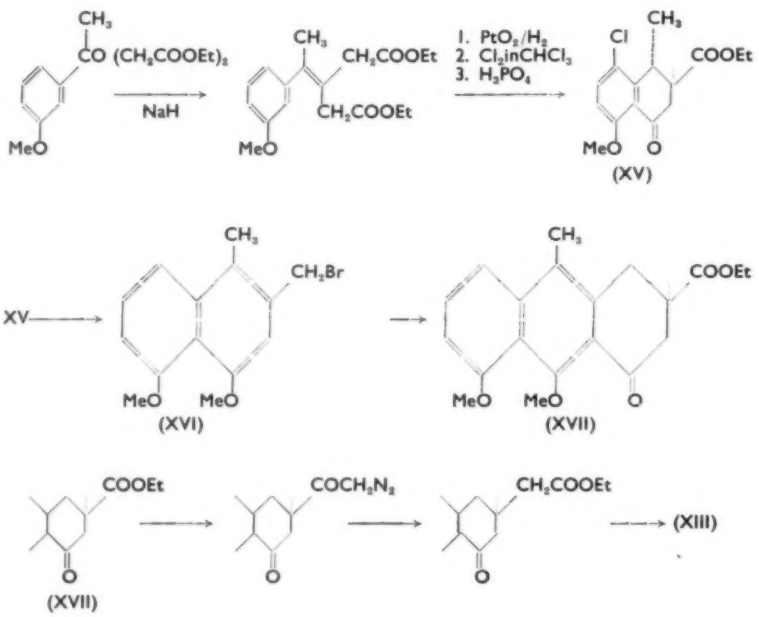
The dehydrogenation of (XV), followed by methylation, reduction, and bromination of the product, gave the naphthyl bromide (XVI), which on successive reaction with carbethoxymethylmalonic ester, cyclisation and decarboxylation, gave the anthracenone (XVII).

The A-ring was similarly generated. By routine methods (XVII) was converted to a diazoketone, which underwent a Wolff rearrangement to give the corresponding homocarboxylic acid; this was esterified and the ester reacted with magnesium malonic ester, and the product cyclised with sodium hydride and then treated with ammonia and demethylated to give (XIII; R CH_3).

Alternatively the ketal of the tetralone (XV) was converted by standard methods to the corresponding homoaldehyde, which was successively reacted with malonic and acetoacetic esters to give the tricyclic (A-CD) compound (XVIII); this was cyclised and then hydrolysed with acid to (XIV; R_1 CH_3, R_2 H).

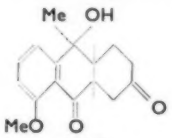


Rather similar methods were used by the American Cyanamid Co. workers to prepare the related *compounds* (XIII; $R = H$)[37] and (XIV; $R_1 = H$, $R_2 = CONH_2$).[38] Since the 12a-hydroxyl group may be introduced into these compounds by oxidation with perbenzoic acid[39] or nitric oxide,[40] they lack only the



4-NMe_2 group of the naturally occurring tetracyclines.

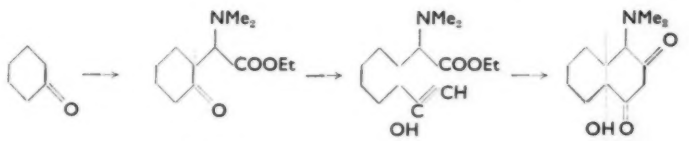
Synthetic approaches by other routes are as yet of lesser importance. It is however worth mentioning the studies of the Moscow group,[41] which indicate a possible method of introducing the biologically desirable 4-dimethylamino group. 2-Methoxybutadiene was added to 5-methoxy-1 : 4-naphthoquinone, and the adduct treated with methyl magnesium iodide and then hydrolysed to give, among other products, the trione (XIX).



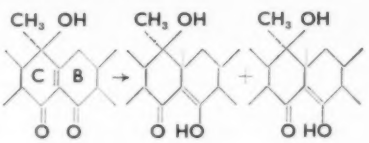
(XIX)

The next steps have so far been studied only in model compounds. Thus cyclohexanone was condensed with ethyl glyoxylate, and the product treated with dimethylamine to give, by an anionoid addition, the α-amino-ester (XX). This reacted with sodium acetylide in the expected way to give a tertiary carbinol, which by acid hydrolysis followed by cyclisation should give the compound (XXI), which is an obvious model for the tetracycline A-ring.

3. The use of mutant strains of the tetracycline-producing *Streptomyces* species. Thus, one such strain produces the very interesting *6-demethyltetracycline* (I R_1=R_2=R_3=H), which has the desirable characteristic of being retained in the body much longer after injection than tetracycline itself.[42] Another mutant yields $\Delta^{5a,11a}$-dehydrotetracycline (XXII), which on reduction gives a mixture of tetracycline and the biologically inactive 5a-epitetracycline.[43]



(XX) (XXI)



(XXII) (I)

Table 1

Compound	*Activity against*[44] Staphylococcus aureus *relative to tetracycline*	*Reference*
Tetracycline	100	42
Modified A-ring		
Tetracycline nitrile	Active (c. 5)	42, 45
4-Epitetracycline	5	29, 42, 46
4-Dedimethylaminotetracycline (VII)	Active	47
12a-Deoxytetracycline (IX)	Slightly active	31
Modified B-ring		
5-Hydroxytetracycline	96	42
*Apo*terramycin (IV)	0	48
$\Delta^{5,13}$-Dehydrotetracycline (XXII)	<1	43
Modified C-ring		
6-Deoxytetracycline (XII)	18	33, 34
6-Demethyltetracycline	96	42
6-Deoxy-6-demethyltetracycline	40	34
Anhydrotetracycline (III)	1 (?)	48, 49
4 - Dedimethylamino - 6 - demethyl - anhydroaureomycin (XIII; R H)	Active	37
Isotetracycline (VI)	0	30
Modified D-ring		
7-Chlortetracycline	400	42
6-Deoxy-7-nitrotetracycline	60	34
6-Deoxy-9-nitrotetracycline	1	34
6-Deoxy-9-aminotetracycline	35	34
Model compounds		
7-Hydroxy-3-methylphthalide	0	48
1,8-Dihydroxynaphthalene	0	48
8,9,10-Trihydroxy-1-keto-1,2,3,4-Tetrahydroanthracene	Active	50

Structure and antibacterial activity

The results of these and other investigations into the relationship between structure and antibacterial activity in this series are summarised in Table 1. Although much of this data has been obtained from none too informative patents and is merely qualitative in nature, we may arrive at certain conclusions. For appreciable antibacterial activity the B, C and D rings and the intact C_{11}-C_{12} diketone system must be present in some form; in contrast the A ring and the C_4-C_7 substituents are not necessary, although their presence may be desirable. Bearing in mind that it is the C_{11}-C_{12} diketone system which is involved in the chelation of metals by the tetracyclines, it seems reasonable to connect the antibacterial and metal-chelating activities of these compounds. It is therefore worth glancing at the effect of metal ions on the biological actions of the tetracyclines.

The following related biological properties of the tetracyclines have been studied in this connection:

Effect on bacteria

In concentrations of 1-3γ/ml. the tetracyclines exert a powerful bacteriostatic influence on both Gram-positive and Gram-negative organisms, such as Staphylococci, Streptococci, *Escherichia*, *Brucella*, *Klebsiella pneumoniæ*, etc., and also on pathogenic *Rickettsiæ*, and on the large viruses of the psittacosis and lymphogranuloma type. At much higher concentrations they have a bactericidal effect on most of these species. The effect of added metal ions is curious. Most of the metals which form complexes with the tetracyclines[26] have no influence, but certain divalent metals, notably ferrous iron, manganese, calcium and magnesium, may, when present in excess, inhibit the bacteriostatic action. The degree of inhibition produced varies with the micro-organism and with the metal used;[51]

thus in the system *P. aeroginosa*-oxytetracycline the molar metal : drug ratio required to permit 50% normal growth is 50-140 : 1 with ferrous iron and 2000 : 1 with magnesium.[52] On the other hand, very low concentrations of these same metals may actually enhance the activity of the drugs; thus the addition of small amounts of manganese increases the activity of oxytetracycline toward *P. aeroginosa* and of chlortetracycline toward *C. cucullus*, while the addition of metal-complexing agents such as sodium citrate inhibits the drugs under these conditions.[53]

Effect on enzymes

The tetracyclines are reported[51,54] to inhibit oxidative phosphorylation, fatty acid oxidation, nitro reduction, and other enzymatic reactions in various *in vitro* systems; their bacteriostatic activity is presumably due to their ability to do this *in vivo*. The addition of large (10 : 1-50,000 : 1) excesses of divalent metal ions is said to suppress the tetracycline-induced inhibition. Once more, however, it appears that the presence of small amounts of these metals enhances, and may in some cases be necessary for, inhibition; thus pancreatic lipase is inhibited by chlortetracycline only in the presence of divalent metal ions, the order of effectiveness being Co> MN>Ca>Mg>Ba.[54] It is interesting to note that certain enzyme systems which are inhibited by metals may be reactivated by the tetracyclines; for example, the beryllium-induced inhibition of rat plasma alkaline phosphatase is suppressed by the addition of chlortetracycline or other metal-complexing agents.[55]

Effect on animal growth

It is well known that the growth of young animals and humans is stimulated by the addition of tetracyclines to their diet. This effect is generally attributed to the general bacteriostatic action of the tetracyclines, but there is some evidence that they also increase the efficiency with which the body extracts the necessary trace elements from food; thus chicks fed on a diet low in manganese or calcium suffer less from impaired growth if concurrently treated with tetracycline.[56]

We may therefore conclude that the major biological effects produced by the tetracyclines are closely related to their ability to react with metal ions. The details of the mechanisms involved are, however, less clear. Any satisfactory theory of tetracycline-induced bacteriostasis, for example, must account for the fact, noted above, that low concentrations of certain metal ions may enhance the activity of the drug, while a large excess of the same ions may inhibit it.

Perhaps the most reasonable explanation of this behaviour is to suppose that the metal in question is vital to the operation of an enzyme system in the micro-organism, and that it can react with tetracycline to form a chelate complex which has a greater affinity for the enzyme than does the free metal ion, but which cannot take part in the reactions of the enzyme. In these circumstances the enzyme will be inactivated. When an excess of the free metal ion is added, however, the complex will be displaced from the enzyme to some extent, and the enzyme will be correspondingly reactivated.

The variation in bacteriostatic power between different tetracyclines may reflect differences in their rates of cellular penetration and their affinity for the enzymes in the bacteria being studied; it seems possible that the values of these variables may be determined by the size, shape and acidity of the tetracyclines.

Clinical uses

The clinical uses of the tetracyclines have already been indicated and have been extensively reviewed elsewhere.[57] They are readily administered—usually in the form of the hydrochloride or other salt—orally or intravenously, and maintain measurable serum levels for 12-20 hr; the 6-demethyltetracyclines are retained for up to 100 hr under the same conditions.[58] Their toxicity is low, and the main drawbacks to their clinical use are diarrhœa, caused by the inhibition of the intestinal flora,[59] and, as is the case with all antibiotics, the development of resistant strains of bacteria. However, it is worth noting that strains of bacteria which are resistant to one tetracycline may succumb to another; thus 12a-deoxyanhydrotetracycline is active against various tetracycline-resistant staphylococcus and streptococcus strains.[60]

The tetracyclines are conveniently estimated by turbidimetric microbiological assay using *Staphylococcus aureus*[44] or *Klebsiella pneumoniæ*,[61] or by various colorimetric methods.[62]

From the commercial point of view, the tetracyclines offer even now an attractive field for research because, as has already been made clear, it is possible to produce by chemical or microbiological methods a wide range of biologically active analogues and derivatives of them which may well prove active against species which resist the parent compounds. Moreover the study of tetracycline-metal-enzyme interactions may lead us to a more exact, and therefore more useful, knowledge of the ways in which enzymes may be selectively inhibited. As a former worker in the field I hope it may prove so.

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(*Continued on page* 483)

STERILISATION OF MEDICAL PRODUCTS

2. Gas Sterilisation

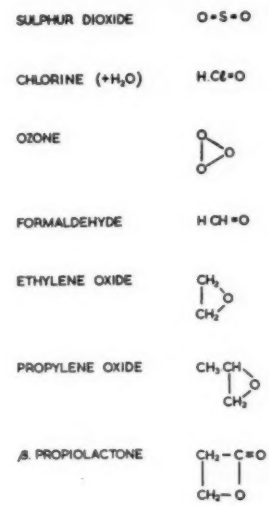
By G. R. Wilkinson*

In the first article Mr. Wilkinson dealt with the basic mechanisms of sterilisation and steam sterilisation in detail. Here he discusses sterilisation by ethylene oxide.

As well as advances in steam sterilisation during the latter part of the last fifty years much more attention has been focused upon the use of gases and vapours for sterilising articles such as wood, plastics, foodstuffs or wool, which cannot be treated by reliable heat sterilisation methods because of damage or modification of the material. The possibility of biological warfare has also directed attention towards non-destructive procedures, particularly for some foodstuffs, and even more recently, now that bodies are being projected into space, to avoid disturbance of the inter-planetary flora, gaseous sterilisation methods have been considered for the scientific equipment carried in rocket vehicles and for the vehicles themselves.

The use of gases for sterilisation and fumigation purposes is not new. The use of myrrh, frankincense and sulphur dioxide can be traced to Biblical times. In more recent days formalin, sulphur dioxide and ozone have been employed in so-called disinfectors used for clothing, bedding and other articles in contact with cases of notifiable diseases. Sulphur candles and formalin disinfection have been part of the armoury of the Public Health Inspector since the 1800s.

* Research Division, Allen and Hanburys Ltd.



SOME MATERIALS TRIED AS STERILISING AGENTS

Table 3. Chemicals containing an active —O— group.

Ideal sterilising gas

For a gas or vapour to be useful in this field of sterilisation an ideal medium would be:

1. A gas or vapour lethal to bacteria.
2. Readily diffusible, readily removable.
3. Have a low toxicity.
4. A rapid action.
5. Be potent in low concentration.
6. Be non-corrosive, non-inflammable, non-toxic, non-irritant, readily available and cheap.

Numerous gases or vapours have been considered over the years and examined for their sterilising properties. These are all highly reactive chemically and they have one common feature, an —O— or other reactive group somewhere in the molecule. It is probably the presence of this grouping which makes them so reactive towards bacterial protein (Table 3).

The effectiveness of some organic compounds as sterilising agents has been extensively investigated, together with the effect of substitution of hydrogen or oxygen in the molecules by other radicles (Table 4).

These investigations have shown that increasing the ring or the size of the molecule causes loss of activity. Conversely, introducing nitrogen, sulphur or halogen into the molecule increases the effectiveness.

It has been suggested that conversion to a glycol is necessary for ethylene oxide and similar gases to exert their effect, but an alternative theory is more likely.

Ethylene oxide/protein reaction

Ethylene oxide can take part in hydroxy-alkylation reactions and it is this type of reaction which is likely to occur with the proteins of bacterial cells and spores. Fraenkel has demonstrated this using ethylene oxide and keratin. Once the protein ethylene oxide compounds are formed, either from the cell protein or an essential enzyme, the vital processes in the cell cease and the organism cannot reproduce itself.

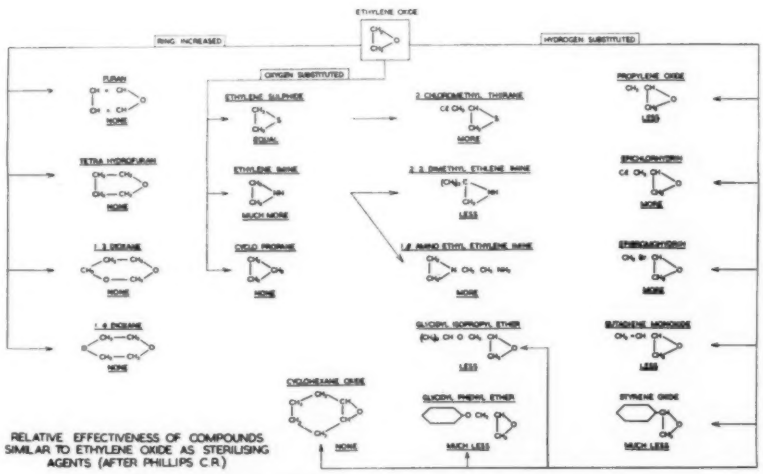
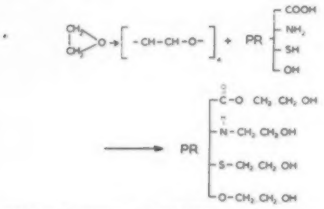


Table 4. Relative effectiveness of some sterilising agents.

The final result is similar to that achieved by heat sterilisation.

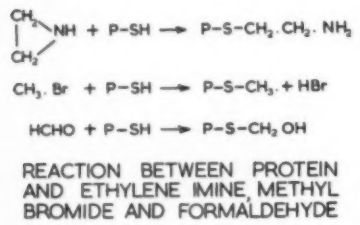
The basic reaction is the replacement of a hydrogen atom in the protein molecule by an alkyl group. The hydrogen may be removed from amino, hydroxyl, phenolic or sulphydryl groups and is attached to the free oxygen formed by the splitting of the ethylene oxide epoxy ring (Fig. 11).



REACTION BETWEEN ETHYLENE OXIDE AND PROTEIN

Fig. 11.

Formalin, ethylene-imine and methyl bromide are believed to act in a similar manner, except that the alkyl replacement group is different. (Fig. 12).



REACTION BETWEEN PROTEIN AND ETHYLENE IMINE, METHYL BROMIDE AND FORMALDEHYDE

Fig. 12.

The removal of such an alkyl group after a reaction of this type is extremely difficult and this could well account for the process being bactericidal and not bacteriostatic.

Most attention has been directed towards ethylene oxide and this will be used as an example. Ethylene oxide is an epoxy compound with two carbon atoms linked with oxygen in a three membered ring and is a highly reactive chemical. It is a gas at ordinary temperature, boiling at 10·8°C., and can be obtained compressed in steel cylinders and in admixture with carbon dioxide or Arcton. In its pure form it is a most dangerous material to handle, as mixed in all proportions with air from 3 to 80% it is explosive. It has a flash point below 20°F. and its auto-ignition temperature is 804°F. When mixed with more than 7·15 times its volume of carbon dioxide, however, it is rendered harmless, and a mixture of 10% ethylene oxide with 90% of carbon dioxide or with Arcton is now available. These may be mixed in any proportion with air without an explosive mixture being formed.

Historical evolution

Historically the evolution of ethylene oxide as a sterilising agent is somewhat unusual. Although mentioned in 1928 by Cotton and Roark as an insecticide, the first reference to the antibacterial activity is in a patent granted to Schrader and Bossert in 1936, who claim that "pests and germs of all kinds" are destroyed by alkylene oxides together with carbon dioxide. Both ethylene oxide and propylene oxide are cited as examples.

In 1936 Kirby, Atkin and Frey reported the control of moulds commonly found in bakeries and were able in vacuum ovens to sterilise loaves which had been intentionally contaminated with spores before being wrapped in waxed paper.

In 1937 a patent obtained by Gross and Dixon gave information concerning the use of ethylene oxide, particularly against bacteria in the presence of moist cotton. Some 48 organisms were tested and complete sterilisation was attained in under 4 hr. at a concentration of about 500 mg./litre. Sufficient moisture was used to convert it to ethylene glycol. Later a preliminary vacuum was included followed by ethylene oxide at 110° to 115°F. for 2 to 3 hr. which was claimed to be successful by C. C. Griffiths and L. A. Hall for gums and gelatin.

About 1938 considerable use was made of ethylene oxide to prevent the spoilage of foods and for the sterilisation of spices. About the same time humidity was shown to play a part.

Griffith and Hall obtained patents on the use of ethylene oxide in a vacuum chamber, together with the introduction of water, again for sterilising spices.

Further patents were obtained for the sterilisation of pancreatin and colloidal material and in 1941 a subsequent patent was granted for the vacuum sterilisation of organic products such as foods, this time without humidification.

In connection with fruits, *B. subtilis* and other sporing organisms were shown to be inhibited, and in 1945 a patent was granted for the sterilisation of foodstuffs packed in cellophane relying on the gas permeability of the plastic to achieve a sufficiently high concentration for sterilisation to occur.

Animal	Effect	Ethylene oxide (mgm/litre)	Time Minutes
Guinea pig	Lethal	80–160	5
	Objectionable	20	30
		5–10	30–60
	Tolerable	10–16	30
		5	60
		2	300
		2	about 400
		0·4	some hours
Rat	Lethal	100	6
		16–20	30
	Objectionable	50	8
		2	300
	Tolerable	50	4
		10	30
		2	440
Mouse	Lethal	10–20	30
		2	300
	Tolerable	2	440

Table 5. Effects of inhalation of ethylene oxide vapour.

In 1942 glass, metal and cloth contaminated with bacteria were shown to be sterile after treatment and consideration was given to the possibility of treating entire railway trains. No details can be found of the outcome of the idea! The same year intentionally infected threads in upholstery were sterilised by a 1:1 ethylene oxide/carbon dioxide mixture, but a concentration of 1:7 failed to sterilise.

In 1943 soil in closed containers was successfully sterilised by exposure to ethylene oxide.

Suggestions were made in articles that plaster of paris bandages could be responsible for the contamination of wound with tetanus, gas gangrene and other organisms; of 194 samples only one was sterile and *Clostridia* were recovered from 132. With the collaboration of Greenberg and Klotz attempts were made to sterilise these bandages, dry and wet, with ethylene oxide. Exposed to high concentrations of ethylene oxide at 37°C. overnight and at pressure of 0·25 atmosphere produced satisfactory results.

It was not until 1950, in the U.S.A., that interest developed in the field of hospital equipment. Linen blankets, both soiled and laundered, from which large numbers of micro-organisms could be recovered, were

SORPTION OF ETHYLENE OXIDE BY VARIOUS MATERIALS

MATERIAL	Amount of ethylene oxide sorbed after 18hr. contact with 10 per cent v/v ethylene oxide in air at room temp. (20°C approx.) mg./g.
Polythene	2
P.V.C.	19·2
Bakelite	Nil
Brown Paper	6·1
Cardboard	10·4
Packing case wood	18·4
Cotton wool (absorbent)	3·5
Cotton wool (non-absorbent)	4·1
Red rubber closures	5·5
White rubber closures	7·4
Black (neoprene) rubber closures	15·2
Starch glove powder	10·5
Kaolin	2·5
French chalk	0·5
Sulphanilamide	0·8
Procaine penicillin	0·2
Water	25–30

Table 6.

completely sterilised by ethylene oxide using a pre-vacuum technique.

Kaye found it to be effective in the sterilisation of penicillin infected with *B. globigii* using a concentration of 475 mg./litre at a pressure of 200 mm. of mercury for 6 hr. No change in potency or toxicity could be detected, but when the same procedure was tried on streptomycin calcium chloride a 35% loss in potency occurred.

Application of the procedure to crystalline materials was considered and a paper published in 1956 indicated some crystalline materials which could not be sterilised by gases due to bacteria being locked in the crystals.

For sterilisation of food products after packaging ethylene oxide and propylene oxide were employed by F. K. Baerwald as early as 1945, but it was only in 1958 the procedure was used for packaged pharmaceutical products. The sterilisation of plastics in paperboard, namely a plastics intravenous injection set in a cardboard box, is now carried out by a very similar procedure.

The use of ethylene oxide for sterilising antibiotics, pharmaceuticals and dressings increased considerably in the U.S.A. until in 1955 nearly as much was being used as for fumigating foodstuffs. The cost is low and at that time was about 4·15 cents/kg. of penicillin.

Hospital blankets were sterilised, using a standard laboratory autoclave with a mixture 10% ethylene oxide in carbon dioxide. A pre-vacuum was found to be necessary. Organisms killed included *Streptococcus hæmolyticus* and spores of *B. globigii*. At the same time a culture of the BCG strain of tubercle bacillus was also rendered sterile.

Moulds were reported to have been killed in packaged foods by fumigation with ethylene oxide and there is evidence that vaccinia and a strain of encephalomyelitis viruses are killed. In these tests no viable viruses could be detected after 8 hr. exposure to the vapour.

Applications

Ethylene oxide is now firmly established as a sterilising agent in industry, but its use in hospitals is developing only slowly in this country, although it is used where no other sterilisation procedure is practicable. It is employed for the sterilisation of plastic equipment such as the heart-lung machine and for bronchoscopes which cannot be subjected to high temperatures, and also for microscopes, ophthalmoscopes, tonometers, spatulæ, instruments and other apparatus used in ophthalmological operations with considerable success at concentrations of 1,250 mg./litre at 70°F. for 4 hr. in admixture with dichlorodifluoromethane without harmful effects upon plastics, rubber, leather and other similar materials.

Similar work on photographic films, swim suits and beauty salon equipment has recently been reported.

The most recently published work on the subject is again by Phillips's team and describes the use of simple chambers such as oil drums, tyre inner tubes and polythene bags. The sterilising and quenching gases are in standard aerosol containers fitted with special valves for easy handling and transport.

These containers contain 11% ethylene oxide, 44·5% Arcton 6 and 44·5% Arcton 9. It is important to remember that this mixture in liquid form is an excellent solvent for some plastics.

Since ethylene oxide is a highly reactive chemical it does not fit the criteria outlined earlier for a perfect gaseous sterilising agent and therefore certain harmful effects can occur if not properly controlled.

When used in admixture with carbon dioxide or Arctons it is safe, and since these mixtures are available they are the only ones which should be considered for small-scale use. This cannot be repeated too often.

Toxic effects

The toxic effects have been studied on small animals and the effects of inhalation of the vapour are shown in Table 5.

The inhalation hazard is due to irritation of the respiratory system, but normally the odour is not sufficient warning. At 20 mg./litre an odour similar to acetic acid is produced.

The vapour is very dangerous to the eyes. High concentrations cause intolerable irritation and even in comparatively safe concentrations there is a distinct effect. This irritation must be taken as a warning, otherwise severe damage can occur.

Computation from animal work suggests that 1 mg./litre for some hours could cause sickness and death, although one authority has suggested a limit of 100 mg./litre as safe for an 8 hr. working day.

In guinea pigs the order in which symptoms occur are nasal irritation, eye irritation, blood tinged and frothy serous exudate from the nostrils, unsteadiness on the feet, staggering and the inability to stand. Later respiratory disturbance, dyspnœa and gasping occur, then death.

There have been reports of men ill after ships had been fumigated, and in one case ten women were overcome in a food factory.

To give some estimate of the human toxicity hazard, it is convenient to relate it to other probably better known materials. It is considered to be less harmful than hydrochloric acid vapour and sulphur dioxide, but more toxic than chloroform and carbon tetrachloride.

When handling the cylinder of gas or using equipment it is advisable to use well-fitting goggles and a plastic face shield. Furthermore, unless the equipment is used in very well ventilated situations suitable respirators should be worn if there is any possibility of escape of vapour into the atmosphere.

Apart from these hazards, ethylene oxide is soluble to some extent in plastics and rubber, and articles made from these materials should be well aired after sterilisation, for if worn immediately high local concentrations are vesicant and may cause blisters or irritation (Table 6).

As will be seen from Table 7 there is conflicting opinion concerning the time of application and concentration of ethylene oxide required for sterilisation.

Phillips carried out a number of experiments using dried cotton cloth

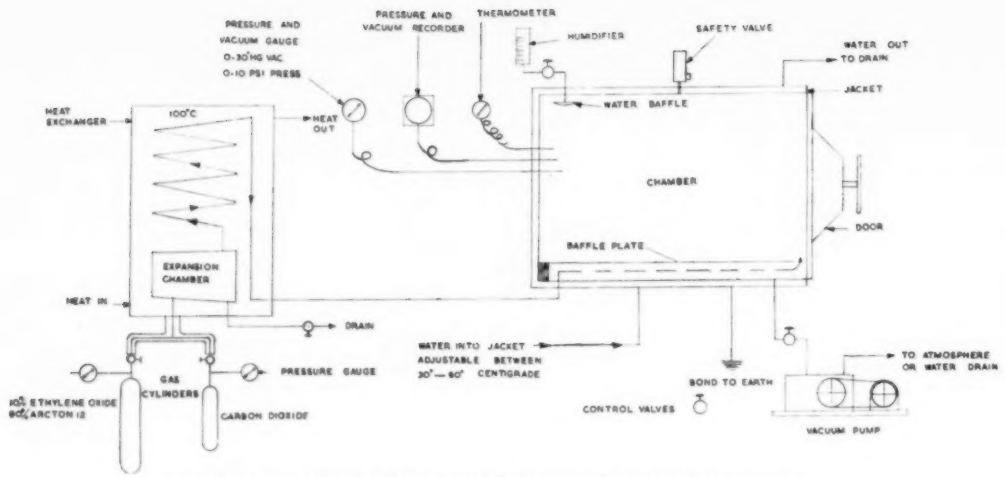


Fig. 13. Schematic layout of ethylene oxide sterilisation unit.

patches impregnated with 5×10^6 *B. globigii* spores at 5°, 25° and 37°C. in stoppered bottles. From the results he was able to deduce the relationship between the death rate and time; this was logarithmic and varied with temperature, the coefficient being 2·74 for each 10°C. based on a 90% kill. The data shown in Table 8 gives the relationships.

For complete sterilisation at a concentration of 90 mg./litre at room temperature (about 25°C.) the times shown in Table 9 were required. It is clear that at room temperature it is not a rapid process and raising the temperature to reasonable limits has little effect.

Equipment

Suitable equipment can be assembled using an orthodox steam steriliser as the chamber, but it is advisable to use equipment designed for the purpose.

The steriliser chamber should be capable of withstanding 33 p.s.i.g and 30 in. Hg vacuum. This will permit the admission of sufficient ethylene oxide/carbon dioxide mixture up to an ethylene oxide concentration of about 500 mg./litre. It should also be jacketed for steam or hot water heating.

The other equipment (Figs. 13 and 14) comprises:

1. *A vacuum pump* capable of exhausting the system to at least 28 in. Hg vacuum within 5 min. and being unaffected by air, moisture, carbon dioxide and ethylene oxide. This pump should have its exhaust taken into the open air.
2. *An expansion chamber* made of, or lined with, stainless steel, fitted with a jacket or internal coil heated by steam.

MATERIAL	ORGANISMS	CONDITIONS		
		$(CH_2)_2O$ mgm/litre	Temperature °C	Time Hours
Moist Cotton	Various	524	—	2·5 to 4
Sugar	Thermophile	717	—	2·5
Tobacco	Normal Flora	893	—	5
Sand, Starch	Aerobic Spores	1,150	85	5
Bread	Mould Spores	176		0·125
Dry Foods	Normal Flora	458	65—110	2·5
Dry Gums	Normal Flora	458	43·5	2·5 to 3
Surgical Goods	Normal Flora	458	87·5	2·5 to 3
Pancreatin	Normal Flora	458	32·5—54·5	2·5
Spices	Normal Flora	1,920	21—32·5	3
— do —	— do —	960	21—32·5	6

After Phillips 1949

Table 7.

25°C						
	CONC. IN % GAS	1·1	2·2	4·4	22	44
	CONC. IN Mgm./LITRE	22·1	44·2	88·4	442	884
	TIME: HOURS 90% KILL	7·2	3·3	1·6	0·5	0·35
	TIME: HOURS 99% KILL	10—24	8	4	1	1

Table 8.

ETHYLENE OXIDE 90mgm./litre 25°C	
B. globigii spores	10 hours
B. globigii	5 hours
Staphylococcus aureus	6 hours
Mycobacterium phlei	6 hours
Gaffjya tetragena	4 hours
Serratia marcoscens	3 hours
Eberthella typhosa	2 hours
Klebsiella pneumoniae	2 hours
Escherichia coli	2 hours

Table 9.

3. *An efficient air filter* for the introduction of air into the chamber after sterilisation, to vent the gas and to air the contents.
4. *Means of introducing water* to produce a suitable humidity.
5. *Automatic control equipment*, although not essential, is desirable as the procedure is complicated.

These units should be connected by stainless steel pipework and the valves should be corrosion resistant.

Method of operation

The following operations can only serve as a guide, as changes may be necessary because of the features previously outlined:

1. Admit into the expansion chamber sufficient carbon dioxide to purge the system. This is only required if air has been allowed to enter this part of the system.
2. Introduce at a suitable rate further ethylene oxide/carbon dioxide mixture. The gas mixture should reach operating temperature before use. This can normally be taken as 40°-60°C. and ensures all the ethylene oxide is in the vapour phase.
3. Apply vacuum to the steriliser with the jacket maintained at 40°-60°C.
4. When a vacuum of 28 to 28½ in. Hg has been obtained introduce sufficient water to produce a suitable humidity when the working pressure has been restored. This can only be determined by experiment and depends upon the load.
5. Introduce the ethylene oxide/carbon dioxide mixture from the

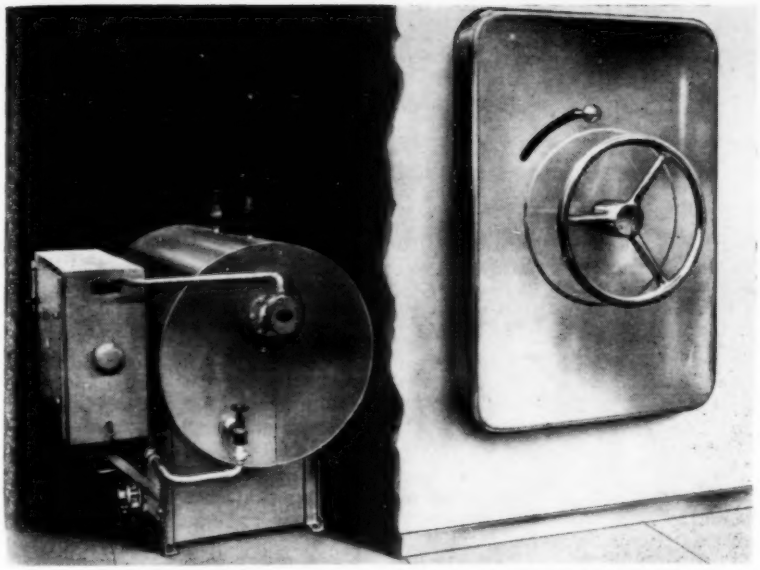


Fig. 14. Equipment used in ethylene oxide sterilisation.

expansion chamber until a suitable positive pressure is developed and maintain at this pressure during the sterilising period, supplementing any pressure drop by adding more gas.

6. At the expiry of the sterilising period evacuate until a vacuum of 28 in. is attained and then introduce air through a suitable filter to remove any residual ethylene oxide.
7. After a suitable period stop the pump and equilibrate the chamber with the atmosphere. Then open the steriliser door.

The obvious method of examining the efficiency of a sterilising procedure is to make use of spore papers, but this is difficult because of the period required for sterility testing. In the field of heat sterilisation physical methods are customary. These are such things as Browne's Tubes or colour change papers and this type of indicator has been extended to ethylene oxide by Royce and Bowler.

These indicators make use of the colour change of bromophenol blue in a solution of magnesium chloride and hydrochloric acid when the ethylene oxide absorbed by the solution is converted to ethylene chlorhydrin and renders the solution more alkaline. The solution is made up in sachets of thin polythene film which is permeable to ethylene oxide.

Conclusion

An attempt has been made to review the present position of gas sterilisation and to put fairly the advantages and disadvantages. At present it is difficult to assess its value and it is necessary for it to be tried for the purpose under consideration in the apparatus to be used before a decision as to its effectiveness can be taken. The procedure is sufficiently temperamental for a paper to be published on the subject of the "Faulty Function of a Table Model Ethylene Oxide Steriliser" saying that experience has indicated that sterility does not invariably result when following the directions.

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(*Continued from page* 478)

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DETERGENT BAR

A milled and plodded detergent bar comprises:

22-40% sodium salt of a substantially saturated higher fatty glyceryl sulphuric acid compound,

3-13% sodium C_{10}-C_{18} alkyl aryl sulphonate in which the aryl radical is selected from the group consisting of benzene and its substitution compounds,

35–50% alkali-metal soap, of which a major proportion is sodium soap, the soap being predominantly of C_{12}-C_{18} fatty acids of which 40-60% are saturated C_{16}-C_{18}, 10-35% are saturated C_{12}-C_{14} and 5-37% are unsaturated,

6-15% moisture and

2-10% water-soluble alkali-metal sulphates and chlorides, the major proportion of which are sodium salts, the amount of sodium chloride present being from 2-7% and that of sodium sulphate being no greater than 5%.

(Australian Pat. Appln. 51,321/59.)

How Market Research Can Improve Efficiency in the Chemical Industries

By Gordon Allen*

The market research worker is a comparative newcomer in the industrial field, his main sphere of activity being in the consumer field. Mr. Allen shows how the collection and interpretation of facts about market conditions can help the chemical industries to plan production and development more efficiently.

IT is the duty of an industrialist to get maximum return on employed capital from any commercial venture, whether it be manufacture, sales or supplying a service. With the development of mass production techniques, mass marketing and an increased level of general affluence, the capital investment required to manufacture and market a mass-produced article or product is normally of the order of several million pounds sterling. The responsibility of executives dealing with shareholders' money in such large amounts is very heavy indeed, so they must use all available techniques to supply information to arrive at correct business decisions. Outstanding among such techniques are work study, cost accounting and market research. Unfortunately, these techniques only define business problems with greater accuracy and greater detail and do not eliminate the need for basic decisions, so the executive's judgment is still the most important factor in maximising profit from an investment. Possibly the most powerful, informative and simplifying of these techniques is market research, as it is concerned with ensuring that no industrial activity is undertaken unless there is a good chance of commercial success.

Market research techniques

Market research is essentially the collection and interpretation of the facts of market conditions which are considered against the background to give the manufacturer or marketer such details as:

1. Size of market and proportion held by each manufacturer.
2. General consumer attitude towards products and/or manufacturers.
3. Future trends and developments and likely impact of them on the market.

This list could continue almost indefinitely, but is probably best summarised by " careful assessment of wants which can be met by the product."[1] Collection of material can essentially be divided into two basic tasks. The first is desk research, namely collection of statistics, analysing economic trends, background reading of a technical nature. Much of this information is already available on company files, but it is the collation of it which gives point to the exercise. After this has been done, or substantially completed, the second task, which is the collection of market information and opinion, can be started. This latter phase is generally expensive, particularly in the chemical industry as it involves employment of skilled personnel with considerable technical training, and even in some cases highly qualified specialists.

The chemical and allied industries are becoming increasingly conscious of the importance of market research. This is underlined by the attendance at the recent summer school of the Market Research Society at Oxford. Approximately one-quarter of those attending (*i.e.* 20 out of approximately 80) represented companies producing raw materials, *e.g.* plastics, chemicals, etc. For convenience, this activity, which includes the chemical industry, is called industrial market research and the Market Research Society have a section dealing particularly with the problems of this group. Membership of the Market Research Society is currently about 750 and has shown a seven-fold increase since 1953. At this recent summer school papers covering most of the applications of market research were given, but the bias was strongly to the consumer field, where most experience has accumulated. The industrial market research worker is fortunate to be able to take advantage of the experience and the techniques evolved for consumer market research, though they have to be modified to meet the different problems of the industrial field.

The problems of a market research worker in a consumer industry, such as detergents, are clearly quite different from those for work in a chemical field, such as adhesives. Investigation in the consumer field is completely dependent on the use of a questionnaire, completed by a properly defined sample of users. Drawing up a questionnaire to avoid questions socially or morally loaded is an art in itself, for example, an interviewer would not ask how frequently a person bathed, but rather, has he bathed today, thus preventing the respondent interpreting his way of life to his favour. Fortunately, in the industrial field, we do not normally have to worry about such loaded questions, but, of course, the worker must be very conscious of the status and size and competitive position of a company contacted. Occasions when the questionnaire is suitable for industrial research workers are rare, particularly in the chemical field. The design of such a questionnaire is simple and is applicable to problems such as how much paint will be used by small boat manufacturers in the next two or three years. A sample of small boat manufacturers of various sizes is drawn up, and a questionnaire can be sent to them or delivered personally by a representative. This brings us right up to one of the major differences between the consumer and the industrial field, where in the former personal contacts are much less important. This arises because the size of the sample taken may be quite large, say several thousands,

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but still is only a very small proportion of the total customers. In the industrial field, however, the number of customers is very rarely over 1,000 and one cannot afford to antagonise or otherwise irritate what amounts to a large proportion of the total number of customers. The market research worker must be tactful at all times and realise when further questioning is not being appreciated. In fact the use of a questionnaire in its formal form can often be a liability.

Basically in the consumer field there are two types of interviewing techniques. Firstly, there is the straightforward approach of waylaying the respondent in the street (having weighed up the socio/economic class and age group), asking some straightforward questions in precisely the order on the questionnaire with an absolute minimum of chit-chat between questions. This is a purely mechanical process, though certain personalities are obviously less " refusal-prone " than others. Even so, relatively low-paid people can be employed to do this job. The second major technique is so-called " depth " interviewing in which a psychologist or person skilled in certain psychological arts visits the homes of people, selected according to pattern of socio/economic status, and spends several hours discussing with them the subject under investigation. The point of these techniques is to get some idea why people reply in the way they do to the questions. This is a powerful tool in analysing the attitude of people towards products and manufacturers, and forming an accurate idea of what the company or brand image is. In the industrial field there is, fortunately, no place for such psychological techniques, interesting though they may be. This however does not imply that the company or brand image is unimportant in the chemical field, and indeed these factors will almost certainly be more important in the future. Assuming a buyer can buy product X from four or five large companies, all extremely sound, all offering the same delivery, same price, etc., why does he buy from one and not another? In general, purchasing is influenced by the policy of the company which comes from the senior executives who direct the buyer. These executives, being very busy men, have little time to study detailed situations and accordingly may be influenced by the brand or company image, as in effect this is a concise summary of the overall situation. This is presumably one reason for the prestige advertisements appearing in the better-class newspapers and technical journals. It is probably more true in the industrial field than in the consumer field that the brand image must have a close relation to reality if it is to last.

Market research information

By skilful collection of information and even more skilful interpretation of this information an accurate picture of the current market situation is obtained, including such points as the size of the market for a particular product, the applications and relative importance, growth rates, the proportion of the market held by various competitors and competitive products and current marketing and advertising activities. From this information it is possible for the marketing executive to see at a glance how his company is currently doing in a particular field, in relation to his competitors, and to formulate marketing plans to take best advantage of the actual market situation.

While market research is extremely valuable as an aid to marketing, it is equally useful in the chemical industry as an aid to forecasting. This is overwhelmingly important to a chemical company considering a major project involving capital of the order of several million pounds, as the plant will probably take two years before coming on stream. Accordingly, the market research workers, or perhaps we should here say the forecaster in the chemical industry, must always have his sights on the period at least three to five years ahead, which starts two years from the current date. In general published statistics, where available, will give a picture of the past, whereas market research techniques give a picture of the present. From the two pictures, past and present, it is comparatively simple to extrapolate into the future if technological progress can be discounted. In general this simplifying assumption cannot be made and the chemical market researcher must anticipate and evaluate technological improvements, even when they are only at the development stage, and estimate the impact they will have on the market. To do this a great deal of detailed knowledge is required, which is gained by wide reading and discussion with research workers in the field, whence a shrewd estimate is possible of how long it will take to complete the improvement, bearing in mind the development effort employed by interested companies. Having decided when the breakthrough can be expected, the market for the new type of product is then evaluated by standard techniques. This point can well be illustrated by an example: if water could be improved by technological advance to boil at 150°C. at standard pressure, though one has never seen such water, it is still possible to predict what market will exist in heat exchangers, solvent extraction, etc.

Because of the uncertainties implicit in forecasting, the claim is frequently made by workers in the industrial field, that the statistics are not important. Rarely there is an uncertainty factor of as much as 30% on a forecast or again it may depend on Government action (always a problem), but figures and figures alone give the mind something to cling to. The accuracy of such predictions is dependent on three factors.

1. Availability of statistical information.
2. Accuracy of the market research investigation.
3. Skill of the person doing the forecasting.

Unfortunately, the first factor—namely, availability of statistical information—should be the simplest and most reliable, but in practice is generally frequently inadequate. Statistics are kept by the Board of Trade, the Association of British Chemical Manufacturers, the Plastics Institute, trade bodies such as the Milk Marketing Board, etc., and these statistics are invariably those which manufacturers are prepared to disclose because they believe in general it will do them no harm. In fact there is less statistical information in the U.K. than in the U.S.A., U.S.S.R. and other countries, which is a considerable handicap to British workers in this field.

In the absence of published statistics, the market research worker has to make an estimate for himself based on information he has gleaned from the industry concerned with the product being investigated. From this has sprung the idea of the market research worker as an industrial spy. Methods which industrial spies are reported to use include placing an agent in the works, counting delivery vehicles, taking aerial photographs to find out the size and capacity of a plant, and catching a dissatisfied

worker in the local pub and filling him with beer to loosen his tongue. Probably these tales have gained in the telling and these events occur but infrequently in the U.K.; certainly these techniques would appear to be more time-consuming and expensive (and very unethical) than the conventional analytical techniques. Certainly no major chemical company or reputable market research bureau would consider employing these techniques.

However, when the market research worker has obtained by one means or another the basic statistical data and the estimated demand for the future, he has to find out the present manufacturing capacity already on stream or planned to come on stream. This he can very rarely do by direct questions, but occasionally it is published. This is particularly true of major petrochemical projects such as ethylene and propylene utilisation. In the absence of published capacities the market research worker collects rumours or gossip which fortunately are usually reliable. Thus if he discovers there has been a particular shortage of a product and the estimated consumption of this product is known, he can safely equate the manufacturing capacity to the consumption, allowing for imported material. However, in the last analysis gossip items can be cross-checked.

This process is well illustrated by example. Assuming estimated demand of product X is 2,000 tons in 1963, and it is known that current manufacturing capacity is 1,200 tons and no planned increased capacity is discovered, there is an opening for further manufacturing capacity of 800 tons. Should, however, the market research worker be misinformed and another company is planning to have operational by 1963 a 1,000 tons per year plant, there will be a situation of gross overcapacity with corresponding inefficient working of two plants. This state of affairs arises too frequently and our industrial leaders should be giving it attention.

Market research and direction of development effort

The market research worker in the chemical industry can also fill an additional valuable function, namely reporting back to development what is required in the market. Development effort in industry should only be applied on projects which will give maximum return, and this may mean a shift of emphasis within a development project as market conditions change. This can really be considered as a bonus obtained from employing a skilled investigator to carry out work in this field. There is always some doubt in industry whether maximum return is obtained from money spent on development, and this is probably one of the best ways of making sure there is minimum wastage. Great emphasis is put on this function in some of the textbooks on chemical market research.[4]

Conclusion

In an earlier paragraph there was reference made to the deplorable lack of statistical information available in the chemical field. At this point it is important to evaluate the significance of this shortage of factual information. Market research is a powerful method of enabling the industrialist to select a process or product giving maximum return on invested capital, *i.e.* operate at maximum efficiency. For social and political reasons it is imperative that we, as one of the leading industrial countries, be fully competitive with other major countries or groups of countries. Statistical data are the raw materials of planning, and without getting too involved in political issues it is almost self-evident the planned expansion of an industry is more efficient than an unplanned expansion because, as illustrated above, if too many factories go into a field and there is a situation of over-capacity, plants are forced to work below optimum output, which involves loss of efficiency both to the companies concerned and to the chemical industry as a whole. This could be a very significant factor in the next decade as the results of the planned development of the Russian and Eastern European chemical industry become apparent on the world market. It is suggested that what is required is a complete change of attitude by British chemical manufacturers, so that they approach the American standards in publishing statistics.

In conclusion it should be said that the *raison d'être* for applying market research techniques is to keep industry working at maximum efficiency. It is not a simple nor an inexpensive tool to apply, as an elementary survey will probably cost over £1,000, though of course this must be viewed against the background of the magnitude of the capital risked in the venture. For the national good, we in the chemical industry must be continually keeping abreast with demand and avoid bottlenecks where our competitors can move in. Market research is still a new field and sometimes the results are suspect. However, it is doubtless true that almost any picture is better than none and the day of backing the businessman's unsupported hunch is over.

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Industry's Publications

Drug intermediate. A data sheet on 2-piperidinoethanol (N-(2-hydroxyethyl) piperidine) is available from Robinson Bros. Ltd., who are making it in experimental quantities. It behaves as a tertiary aliphatic amine and as an alcohol.

Biochemical materials. A comprehensive catalogue of B.D.H. biochemicals has been published. The list has been enlarged and rearranged so that grouped lists of materials—carbohydrates, enzymes, lipids, etc.—are followed by an alphabetical list of containers, prices and specifications. Many of the additional items are steroids and related substances.

Industrial and agricultural chemicals. Hooker Chemical Corp., U.S.A., have issued a new quick-reference catalogue of their organic and inorganic chemicals.

B.D.H. catalogue additions. A pamphlet describing new entries in the B.D.H. catalogue has been issued. These include glyoxylic acid, ester wax 1960, DL-glutamine, high purity metals (antimony, arsenic, lead and tin), imino-diacetic acid, imino-diacetic acid disodium salt and the B.D.H. Lovibond Nessleriser.

Gas engineering. The products of the gas atmospheres division of the Incandescent Heat Co. Ltd. are described in a new leaflet. These include bog ore boxes, gas burners, butane burners, scrubbers and storage vessels, and waste gas processing equipment.

Pharmacy's International Parliament

By S. J. Hopkins, F.P.S.

At the 18th general assembly of the International Pharmaceutical Federation in Copenhagen, subjects as varied as enzymes and trade marks were discussed by the delegates who between them represented 33 countries. Here are some first-hand impressions of this international parliament of pharmacy.

AT THE opening session in the Tivoli Concert Hall, at which the King of Denmark was present, Professor Niels Bohr, President of the Royal Danish Academy of Sciences, spoke on the close relationship and dependence between the knowledge of all the sciences, the immense complexity of biological systems, and the ultimate need for a balanced approach to integrate research and attack on natural problems. This section concluded with a presentation of gold medals to Dr. J. Buchi (Switzerland) and Professor Schou of Denmark.

Enzymes

The Scientific Section opened with a symposium on enzymes, with reference to their physico-chemical properties, standardisation and assay. At another meeting the principle of non-competitive inhibition of enzymes as a basis of drug action was developed by J. Riehl (Germany). Detoxification mechanisms, the action of cytostatics and antibiotics and their association with enzyme systems was also discussed. Drug resistance, tolerance as well as addiction, may also be capable of interpretation on the basis of enzyme activity.

Small-scale manufacturer

During the Section of Hospital Pharmacists meetings a number of papers were read on the presentation of medicaments in various single dose forms. A detailed examination of a range of theoretical considerations governing the formulation of eye-drops was given by K. Münzel (Switzerland), and these considerations were extended to the practical applications of such factors to both small-scale and batch manufacture.

The production of ampoules, tablets and other single-dose forms of drugs is a common activity of hospital pharmacists, and the range may be wider, although smaller in bulk, than a number of manufacturing houses. This may raise problems of identification. Manufacturers use marked tablet punches, as they work with large batches that make such special punches an economic proposition, which can hardly apply to hospital production. An extended use of foil wrappings, printed if necessary with the name of the drug, was advocated by G. Pirani (Italy), both as a form of presentation and a guard against possible errors.

Safety

At other meetings of the Hospitals Section methods of recruiting staff, which in some countries is on a basis of competitive examination, were reviewed, and also methods of controlling the distribution of drugs in hospitals. Control systems are essential to prevent error and misuse, the hoarding of excessive stocks in wards, and to assist in efficient allocation of expenditure, but should be as simple as local conditions permit, consistent with adequate checks. The importance of safety measures to guard against errors of dispensing as well as use was emphasised in several papers. In some Portuguese hospitals considerable use is made of colour in pharmaceutical preparations, and this was criticised by a number of speakers during the subsequent discussion.

The industrial section held a symposium on pharmaceutical technology and a discussion on a report on trade marks and free names for medicinal substances.

The symposium dealt mainly with methods of extending drug action, and reference was made to the coating of tablets with resistant substances, by D. Jack (Great Britain) to slow-release bases by J. Cooper (U.S.A.), and to ion-exchange complexes as therapeutic agents by L. Saunders (Great Britain).

Trade marks and free names

In the report on trade marks presented by C. C. Stevens (Great Britain), it was pointed out that trade marks not only identified a product but could also guarantee quality. Free names carried no such implication, and the extensive use of free names could undermine trade-mark rights. The two types of names were devised for two different purposes, and industry should see that free names did not acquire the function of trade marks. The Report emphasised that it is unnecessary and undesirable to coin free names for new substances until the value of the substance had been confirmed, as many new compounds had but a short therapeutic life. Amongst other proposals it was suggested that only the W.H.O. should be the authority for approving and issuing free names.

In the subsequent discussion, Professor Bullock explained the attitude of the Pharmacopœia Commission, which preferred to fix free names before the drug was placed on the market. The opposite point of view was expressed by Professor Schulz (Berlin), who considered that a free name should be given after a period of two years as a mark of a successful drug.

Dispensing problems

The problems associated with the distribution of drugs in retail pharmacies as well as hospitals attracted wide attention, and the Commission of Retail Pharmacists was also concerned with the importance of ensuring that all dispensing was controlled and channelled exclusively through the pharmacist. Further discussion in this Section dealt with the technical and professional independence of those pharmacists who do not own the businesses in which they are employed, as the prerogatives and responsibilities of the pharmacist are personal, and cannot be assigned to or taken over by others. The professional aspects of pharmacy and the essentials of a worthy profession were also the subject of an address to a general assembly of the Federation by Professor Schou (Copenhagen).

At another general meeting which was held in Malmo, Sweden, under the auspices of the Swedish Pharmaceutical Society, a report on the effects on retail practice of the

(*Continued on page* 495)

Corrosion-Resistant Plant and the Control of Corrosion

Biggest Exhibition of its Kind Open at Olympia, London, from November 29 to December 2

More than any other industry the chemical industry is bedevilled with corrosion losses. At Olympia the answers to most corrosion problems will be on display when Sir Alexander Fleck, F.R.S., President of the Society of Chemical Industry, opens the Corrosion and Metal Finishing Exhibition, sponsored by the Leonard Hill journal "Corrosion Technology." Covering over 50,000 sq. ft., the exhibition is the biggest of its kind ever held in Europe, and probably the world. You, as a reader of "Manufacturing Chemist," can visit the Exhibition free of charge by using the ticket enclosed with this issue or by presenting your professional card at the turnstiles. To help you in your tour of the Exhibition, here is a pre-view of exhibits.

The Corrosion and Metal Finishing Exhibition, sponsored by "Corrosion Technology," 9 Eden Street, London, N.W.1, will open at 11 a.m. to 6.30 p.m. on Tuesday, November 29, in the Empire Hall, Olympia, London, W.14. On the following Wednesday and Thursday it will be open from 10 a.m. to 6.30 and on Friday, December 2, the last day, it will open at 10 a.m. and close at 4.30 p.m.

Symposia arranged by the Plastics Institute and the Corrosion Group of the Society of Chemical Industry will be held at the Exhibition on the afternoons of Tuesday, November 29, and Thursday, December 1, respectively. Papers to be read and discussed at the Plastics Institute symposium are "Protective Packaging—Engineering Applications" (G. Gonda), "Plastics as Heavy Protective Coatings" (N. Vinson), and "Fabricated Plastics and their Rôle in Combating Corrosion" (K. V. Pepper). Subjects at the Corrosion Group symposium will be "Influence of Water Movement on Corrosion: Ferrous Materials" (Dr. G. Butler of the National Chemical Laboratory) and "Influence of Water Movement on Corrosion: Non-ferrous Metals" (Dr. N. V. Nowlan of the Admiralty Materials Laboratory). The symposia are, of course, open to visitors.

Film shows will also be held throughout the Exhibition.

In the following pre-view, exhibits are classified into functional groups. The comprehensive catalogue and Buyer's Guide available at this Exhibition (2s.) will give quick reference to all stands and exhibits.

PLANT, EQUIPMENT AND MATERIALS OF CONSTRUCTION

Corrosion-resistant pipes, ducting, *etc.*, made from high-density polythene, *Kralastic* and PVC will be featured by *A.B.D.I.C. Ltd.*, as well as PVC and polypropylene valves, tanks and tank linings.

Tanks, vessels, pipe installations, fume extraction ducting and laboratory equipment made from PVC, polythene, polypropylene and *Fibre-Vinyl*, a combination of sheet PVC and polyester glass fibre will be shown by *A. C. Plastic Industries Ltd.*

British Aeroplane Plastics Ltd. will have on their stand pipes made of epoxide resins reinforced with glass and acrylic fibres. Reinforced tanks of glass fibre and synthetic resins will also be shown.

Chemical plant made of cast iron and steel lined with glass enamel will be featured by *Cannon (CP) Ltd.*, who also offer a re-enamelling service for existing equipment.

Chemidus Plastics Ltd. will show their range of pipes and fittings fabricated from unplasticised PVC. A new grade of this material has recently been developed mainly for the water and gas industries.

A consultancy service on corrosion problems is available from *Corrosion Technical Services Ltd.*, who manufacture a range of chemical-resistant cements, sealers and coatings and fabrications of glass-resin laminates.

Rigid thermoplastic pipes will be featured by *Durapipe and Fittings Ltd.* The materials of construction are high-density polythene, styrene-butadiene-acrylonitrile, and rubber-modified high-impact PVC.

Enamelled Metal Products Corporation (1933) Ltd. will exhibit a glass-lined steel dryer-blender suitable for processing highly corrosive materials. A small *Pfaudler* reaction vessel will also be shown.

A section of an industrial fume stack will be used by *Fibreglass Ltd.* to demonstrate the use of reinforced plastics.

Fabrications of PVC and examples of glass/polyester phenolic sandwich construction for thermal insulation will be displayed by *A. E. Griffiths (Smethwick) Ltd.*

The Metals Division of *Imperial Chemical Industries Ltd.* will feature the applications of titanium, which is highly resistant to most forms of chemical attack. The Plastics Division will deal with the uses of vinyl polymers, polythene and polypropylene.

Nordac Ltd. will display pipes and tanks lined with natural and synthetic rubber and will demonstrate the technique of lead lining.

Chemical process plant and pipework fabricated from unplasticised PVC and various laminates will be on the stand arranged by *Plastic Filters Ltd.*, who will also feature polycarbonate transparent sheeting.

Fans, valves, pipelines, *etc.*, constructed of PVC, polythene and acrylics will be displayed by *Rediweld Ltd.*

New developments to be shown by *Saunders Valve Co. Ltd.* include a rubber-lined non-return valve and a solid PTFE valve. This company's range of valves for corrosive materials uses as materials of construction neoprene, ebonite, lead, titanium, nylon and polythene.

Valves of several different types and spray nozzles made of corrosion-resistant materials will be shown by *Meynell and Sons Ltd.*

Chemical plant and tanks lined with lead will be shown by *Aug. Schnakenberg and Co.*, who have developed a process for the continuous lining of steel pipes with lead without an intermediary layer of tin. Fabrications of rigid PVC and polythene will also be displayed.

Semtex Ltd. will exhibit tiles laid in various anti-corrosive cements, glass linings, and an epoxide-based material for anti-corrosive flooring.

Tubing, high-pressure hose and injection mouldings made of nylon will be found on the stand organised by *Tecalemit Ltd.*

A large tank and plastic fans will be used to demonstrate the *Tufplas* tech-

nique of industrial fabrication of plastics by *Tough Plastics Ltd.*

As well as copper-based alloys, *Yorkshire Imperial Metals Ltd.* will display tubes and fittings of polythene and PVC.

COATINGS AND LININGS

Coatings based on epoxide resins, neoprene, *Hypalon*, epoxide/pitch combinations, *etc.*, are supplied by *Brook-Blast Ltd.*, who also operate a service to provide the necessary shot-blasted surface on the substrate.

BTR Industries Ltd. will show examples of linings of soft and hard natural and synthetic rubber, PVC and PTFE, and sprayed and brushed coatings of PVC, neoprene, *Hypalon*, and epoxide resins, as well as pipes and other fabrications made of plastics.

Strippable plastic coatings applied cold or by hot dipping will be featured by *Croda Ltd.* *Metacon*, a new rust remover which will de-rust metal surfaces even though they may be covered with grease or oil, will also be exhibited.

A soft rubber lining to be shown by *Dexine Rubber Co. Ltd.* for use with chlorinated liquors overcomes problems of cracking. Diaphragm valves of cast iron with hard rubber lining and of all-plastics construction will also be displayed.

Plastic-coated steel sheets for industrial buildings have been developed by *Dorman Long and Co. Ltd.* in conjunction with *G. A. Willis Ltd.*, who supply the PVC coating material.

The stand of *The Dunlop Rubber Co. Ltd.* will cover the protection of chemical equipment with natural and synthetic rubber and the use of polypropylene/rubber laminate and chemical brick linings.

The applications of PVC tape in the protection of pipelines will be shown by *John Gosheron and Co. Ltd.* Two new tapes have been developed for the protection of highly finished surfaces during production, storage and transportation.

Penton, a new chlorinated polyether of high molecular weight made by *Hercules Powder Co. Ltd.*, has good chemical resistance at temperatures up to 200° to 220°F., at which it retains its mechanical strength. It is available in sheet form for lining tanks, and metal parts may be coated by spraying, dipping, *etc.*

Plastic coatings and linings manufactured and supplied by *James Lithgow (U.K.) Ltd.* under the name *Calvinac* cover a wide range of composition, according to the particular application. Spraying techniques make it possible to coat the internal surfaces of 35 ft. lengths of pipe in diameters down to 1¼ in. bore.

Metallic Surfaces Research Laboratories Ltd. specialise in metallic coatings applied by non-electrolytic methods such as diffusion, vapour deposition and chemical conversion.

Sprayed PVC finishes and other plastics coatings will be the theme of *The Plasinter Co. Ltd.* stand.

Techniques have been developed by

A tough job of corrosion protection is performed by the *Colvinæ* plastic coating of this crane grab. The material it is shifting is unstoved salt with a 3% moisture content. The coating is supplied by James Lithgow (U.K.) Ltd.

Plastic Coatings Ltd. for the application of plastics coatings by spray or dipping to objects up to 17 ft. by 7 ft. by 7 ft. and up to 5 tons in weight.

Laminated PVC sheet, *Pe Ve Ceal*, is used for lining mild steel tanks by *Plastic Constructions Ltd.*, who will also feature on their stand chemical plant fabricated from plastics materials.

Synthetic coatings and linings for pipework and plant will be featured by *Prodorite Ltd.*, who also manufacture a range of corrosion-resisting cements under licence from Farbwerke Hoechst A.G.

A range of liquid-applied self-curing synthetic rubbers have been developed by *Protective Rubber Coatings (Bristol) Ltd.* under the name *Limpetite*, which are characterised by high non-permeability, bond strength and resistance to abrasion and chemical attack.

Linings of natural rubber, neoprene, butyl rubber and *Hypalon* are applied to chemical plant by *Redferns (Bredbury) Ltd.*, who also supply resin-glass fabrications.

Winn and Coales Ltd. will give special emphasis to their contracting service, which makes available to clients an advisory and labour force for the practical application of *Denso* products to pipelines, structural steelwork, *etc.*

The *Lanshield Sakaphen* range of protective coatings offered by *Wolseley Holdings Ltd.* includes grades with high anti-scaling and non-sticking properties and resistance to nuclear penetration.

A zinc-rich coating which can be applied to steel by brushing, spraying or dipping and dries to a film containing 95% zinc will be shown by *C. and P. Development Co. (London) Ltd.* under the name *Rust-Anode*. Other products displayed will include *Capella* chemical clearer for metal surfaces and *Skaline* mill scale remover.

The *Donald Macpherson Group of Companies* will show coatings based on epoxide resins, *iso*cyanates, and acrylates and paints specially formulated for application by electrostatic units.

Panels illustrating the *Adcora* range of coatings and high-build inhibitive primers will be displayed by *E. and F. Richardson Ltd.* Individual members of this range are based on neoprene, *Hypalon*, *Viton*, polyethers, polyurethanes, and coal tar/epoxide resin.

Antifouling coatings, including *Detel Marina*, will be featured by *Detel Products Ltd.* A zinc-rich primer claimed to be "non-packing" and to require a minimum of stirring before use will be demonstrated.

MISCELLANEOUS

Albright and Wilson (Mfg.) Ltd. will demonstrate with a working model of a condenser cell the ability of *Hagafilm* to promote dropwise condensation of steam and prevent corrosion in steam-heating installations. As well as chemicals for water treatment, they will show chemically deposited nickel plate and nickel-plating solutions.

The theme of the exhibit arranged by *The Geigy Co. Ltd.* will be the importance of quite small amounts of organic chemicals in metal treatment and finishing processes, *e.g.* wetting agents, sequestering agents, corrosion inhibitors and de-watering agents.

In the *Toxion* system for the protection of ships' hulls, to be featured by *F. A. Hughes and Co. Ltd.*, corrosion is prevented by cathodic protection and fouling is avoided by the discharge of a poison underwater.

As well as demonstrating the use of cathodic protection for preventing rusting of submerged piles, *Metal and Pipeline Endurance Ltd.* will show a holiday detector for testing coatings and wrapping on pipelines.

Corrosion surveys are undertaken by *Soil Mechanics Ltd.* as part of a complete site investigation programme, including field and laboratory tests.

Metallic lead pigment made by *Spelthorne Metals Ltd.* is used in paints, plastics, rubber and greases.

An electroplated finish consisting of a tin-nickel alloy will be featured by the *Tin Research Institute*. Reflectors plated with this alloy are being used in the infra-red drying of paint, because of the ease with which deposited paint spray is removed.

On the *MacCleaster Chemical Co. Ltd.* stand, the heat-resistance of *Dox-Anode*, a cementiferous zinc formulation, will be demonstrated by heating a coated panel to 600°C. and shock-chilling in cold water. Also on view will be *Fer-Anode* "liquid zinc," which is used for the protection of ships' hulls below the water line. *Dox*, a rust-removing passivating fluid, finds application in paint spraying shops.

Anti-corrosion packaging will be offered by *Joseph Chadwick and Sons Ltd.*, including case liners. A demonstration of the effectiveness of vapour phase inhibitors will be given.

Efficient Size Reduction

New and Well-tried Ideas in Grinding and Milling Plant

Turbo-colloid Mills

THE Moritz Chemical Engineering Co's. turbo-colloid mill agitates and pulverises products by percussion and shearing. The rotor and stationary crown, placed at a suitable height in the vessel, create an upward or downward circulation of the product to be milled. The rotor consists of centrifugally impelling vanes and two concentric rings of segments which revolve quickly between corresponding segments on the crown. The clearance between rotor and crown may be adjusted within fine limits. This is done to compensate for wear on the milling faces when the milled products are slightly abrasive.

The mills comprise a totally enclosed motor, the body of the mill with its milling elements, a gland to protect against possible flooding, micro-metric adjusting device, jacketed vessel in which the product can be either heated or cooled, and pipes for inlet and outlet of the product.

Four types of mills are made, A, D, P and M, with vessel capacities ranging from 1 to 110 gal. Type A is recommended for processing fluid or semi-fluid solids into which solids or liquids are to be dispersed, type D for viscous products and those that have not to be repeatedly recirculated, type P for products of high viscosity premixed if necessary in another vessel, and type M for products that are not very fluid or have to be recirculated several times through the milling elements.

The mills can be constructed in cast iron, mild steel, bronze, stainless steel, monel, etc.

No. 1 size British "Rema" high efficiency air separator—a test being carried out on the separation of powder.

The Moritz finishing mill. A special steel cone revolves inside a stationary cone also in special steel but of a different alloy. A jacket surrounds the milling head for circulating water or brine. A pump forces the products out of the rotary cone to a certain height and the degree of clearance of the cones is adjustable so that the product fineness can be controlled as well as compensating for any possible wear.

Superfine Milling

The British "Rema" Manufacturing Co. Ltd. manufactures an air separator which, used in conjunction with their ball mills and pinned disc mills, ensures the production of very fine powders. The material flows rapidly through the mill to the separator, where "fines" are extracted automatically, while rejects are returned to the mill for further grinding. Where, however, the mill is operating in conjunction with the air separating system, the finest powders may be produced economically, at high output rates, as no fine material is permitted to remain in the mill, but is treated by the separator almost instantaneously. Also, because of deliberate arrangements made for only medium grinding by the mill, the ball charges required are minimal, resulting in low power requirements.

Used in conjunction with the ball mill, the separator completes a grinding and separating system particularly suitable for producing finished powders of a fineness 75% through 200 B.S.S. to 99·5% through 300 B.S.S. Material particle size is clearly differentiated by the separator, sufficiently fine material being extracted automatically and delivered through the "fines" outlet chute. The separator is totally enclosed and may be driven by vee ropes from an individual motor. It is self-contained, no separate fans, cyclones, air filters or similar apparatus being required. Apart from the special suitability for powder production described for the air separator, in conjunction with grinding mills, the plant is economical for treating free-flowing materials to produce superfine powders. This system is suitable for dealing with only dry materials, so that any appreciable moisture should be removed before the material is introduced.

Air-swept ball mills are manufactured in various sizes for use wherever the process calls specially for this type of plant. The mill has, however, only limited scope, and is uneconomical for very wet material, or if the powder is required to a high degree of fineness.

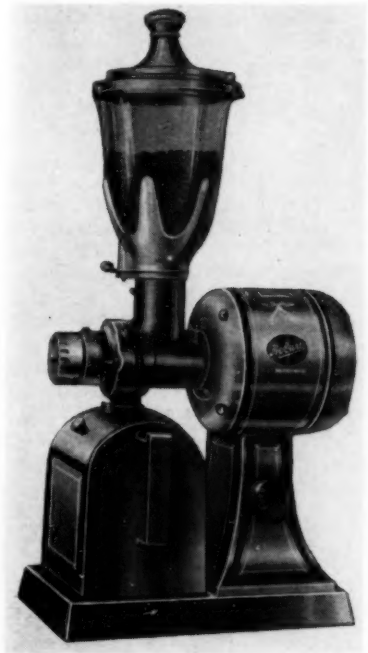
British "Rema" Pinned Disc Mills (Class A) are suitable for the

grinding of friable or medium-hard substances of free-flowering nature, materials in crystal form, many drugs and roots of fibrous character and certain classes of synthetic materials, reducing them to a fine or superfine powder between the limits of 70% through 200 mesh and 99% through 300 mesh.

The class B mills are also employed for dealing with friable or medium-hard substances, generally to produce relatively coarse to fine ground material, *e.g.* colours, oxides, chemical products, food preparations and materials liable to soften or melt at low temperatures. The class B mill is suitable for materials tending to stick or build up.

The fineness of powder produced is usually in the range of 70% through 100 mesh to 95% through 200 mesh, though fine chemicals can, owing to their friable nature, be produced to finer mesh.

Circular rows of pins fitted to the stationary disc are situated between rows of similar pins mounted on the rotating disc. Material fed in at the centre of the discs is propelled in a spiral path to the periphery of the discs passing between the alternate rows of stationary and rotating rows of pins, thus receiving repeated impact action.



Model E2120 grinder made by the Hobart Manufacturing Co. Ltd. has applications for small-scale grinding in the laboratory.

Grinding machines by W. S. Barron and Son. (Top left) The Pep mill for the smaller user. (Top right) No. 7 impact grinder. (Bottom left) No. 5 impact grinder. (Bottom right) Type D.P. Dreadnought grinder.

Laboratory Grinder

For a wide range of rough work in the laboratory Model E2120 made by the Hobart Manufacturing Co. Ltd. gives a grade output at a rate of 0·5 kg./min. The motor is a $\frac{1}{4}$ h.p. available for A.C. or D.C. and is specially designed to take sudden overloads.

The rotating and stationary burrs are of cast chromium alloy accurately ground and lapped to permit close adjustment. A handwheel adjusts the grade of grinding. A safety device is in the form of a copper disc which immediately shears on stone or nail being passed through the machine and allows the shaft to run free, thus preventing damage to the burrs or motor.

Impact and Stone Grinders

The latest machine from W. S. Barron and Son Ltd. is the No. 7 impact grinder which utilises the grinding members of three No. 4 impact mills mounted on one spindle.

Motors of up to 150 b.h.p. can be used. The feed can be either of the *Shaker* or *Vibra* type, the former incorporating a magnetic scavenging plate to remove tramp metal, and the stock is equally distributed over the complete range of beaters. The interior of the mill can be inspected by opening two top half hinged covers, and consists of preliminary grinding plates of novel design in the top half of the mill, and a screen chamber in the lower half incorporating six individual screens. These screens are separated by grinding or spacer plates which prevents the feed from " wandering " and gives each screen a constant load.

Fineness of the product is governed by the mesh of the screen used in the mill. The screens are flexible high carbon steel, and can be inserted or withdrawn from the exterior of the mill by permanent screen handles fitted with a locking device. This can be done while the mill is operating. A smaller model impact grinder is the No. 5.

Also in production is the Type D *Dreadnought* stone grinder. It consists of two grinding stones, one fixed and the other rotating, inside a substantial cast iron casing with bed. The mild steel spindle (sizes 36 in. and 30 in.) on which the revolving stone is fixed is mounted on three long gun-metal ring oiling bearings, the end pressure being taken by a heavy type ball thrust bearing, the pressure being applied by a fine cut screw with lock nut, through two spiral springs, so that foreign materials can pass through the mill without damaging the grinding faces or breaking some other part of the machine.

For finer work the Type D.P. disc grinder will reduce soft and semi-hard stone, minerals and chemicals to a very fine product. The action is basically a rubbing and pressing one, with the plates so designed that a large proportion of the load of attrition is in the material being ground to increase the wearing life of the grinding discs.

The machine can also be fitted with water sealing glands for wet grinding.

Improved Ball Mills

Researches by Dr. H. E. Rose and Dr. R. M. E. Sullivan of King's College, London, suggest that rates of grinding of fifty, or even more, times that attainable in the normal commercial vibrating ball mill can be obtained by a moderate increase in the speed of rotation of the out-of-balance weight shaft of the mill.

An attempt to exploit this latent capacity by a mere increase in the speed of driving of a conventional mill would, however, at once introduce great mechanical problems and there is no doubt that the effective exploitation of this possible increase in the speed of operation of a mill demands radical changes in the basic design of the machine. A study of the theoretical considerations governing the rate of grinding suggests that improvements may be sought by operation at or near resonance and by improving the internal efficiency.

To achieve a high rate of grinding, operation of vibration mills at high frequency is essential. In a large mill the bearing loads and bearing friction losses become prohibitive. This obstacle may be overcome by operation at resonance. Ideally, exactly at resonant speed, the bearing load is zero and friction losses very small, practically some departure from the ideal would be required. Such operation requires the use of stiff or strong springs. Indeed, the springs are the probable limitation on what can be achieved by this method. Overall efficiencies of between 65 and 75% are feasible and would show a substantial improvement over many types of mill available at the present time.

The largest possible fraction of the energy absorbed by the mill charge should be converted to energy associated with new surface. Theoretical equations show that use of grinding media of the highest possible density are required. Similarly, it is considered that there is an optimum mill filling ratio and also

The Pulmac high-speed pulveriser made by Follsain-Wycliffe Foundries Ltd.

that the powder filling ratio has an effect on efficiency.

The type of motion imparted to the mill is important and a circular motion has been found to give a rate of grinding 20 times greater than the same amplitude of motion in a wholly horizontal plane.

This work, which is described in the N.R.D.C. Bulletin, October 1960, is the subject of patent application 2365/59.

High-speed Pulverisers

The *Pulmac* pulveriser made by Follsain-Wycliffe Foundries Ltd. is designed to fine grind a variety of materials at high-speed. It can produce products ranging from granules to impalpable powders.

The grinding takes place between a wear resisting rotor and stator. The angle and spacing of the rotor and stator lugs are critical.

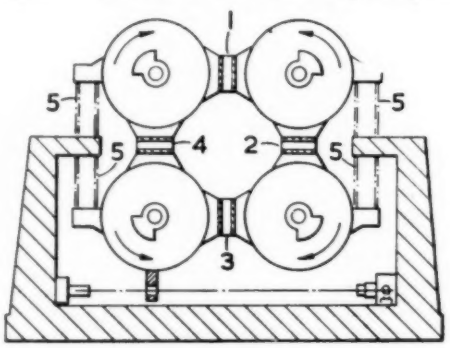
The material is fed into a hopper driven by a belt from the rotor shaft. The feed is *via* a controllable sliding gate on to an oscillating tray which directs the material into a chute which is integral with the pulveriser door into the centre of the spinning rotor. The material is then projected at high speed, imparted to it by the spinning rotor, against the serrated rings in the stator, so there is a combined beating, shearing, crushing and grinding action. Centrifugal force, assisted by air induced by the high-speed rotor, draws the material to the periphery of the rotor where it is ejected through the screens. As it is forced from the centre to the periphery, the material is reduced systematically by the grinding action of the rotor and the attrition of the material beating against itself. The degree of fineness is controlled by the closeness of the rotor and the stator and the mesh size of the screens, which vary from 0·1 mm. to 1 cm.

High Velocity Air Mill

A mill using a new technique has been produced by Russell Constructions Ltd. By generating vortices of air at high velocities and causing their paths to intersect, the particles of a material are made to bombard each other, bringing about rapid and complete disintegration, particularly of difficult products such as those of a fibrous nature.

The mill chamber is a hollow steel cylinder mounted vertically on a rigid base, having a diameter of $13\frac{1}{4}$ in. and a height of 18-24 in. A rotatable co-axial shaft is disposed within the chamber and mounted rigidly upon this shaft is a series of paddles. There is a clearance of $\frac{1}{16}$-$\frac{1}{8}$ in. between the leading edges of the paddle blades and the internal wall, which has a serrated surface. The paddle blades are disposed at intervals of $2\frac{3}{4}$ in. at their tips. The top closure of the chamber carries the shaft bearing, a heavy duty twin ball race, and the delivery outlet and also houses an expeller fan mounted on the shaft.

The machine is powered by a 15-20 h.p. electric motor vertically mounted alongside the chamber, a five-fold V-belt drive imparting a



The diagram shows four mills arranged to vibrate in anti-phase. By this means, the disturbing force acting on the frame is minimised. 1, 2, 3, and 4 are the primary or stiff suspension. 5 are the secondary or soft suspension.

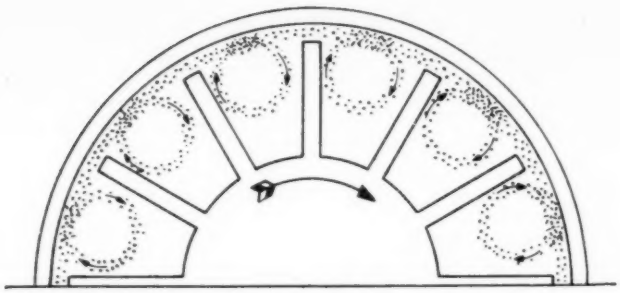


Diagram showing path of particles through the Russell mill and disintegration at the points of intersection.

speed of about 5,000 r.p.m. to the paddle shaft. Directly coupled to an extension of the motor shaft is a blower, the delivery of which is ducted directly into the base of the chamber. The product is fed into the blower and the airborne material is delivered under pressure into the base of the chamber, where it is entrained by the fast rotating paddle assembly.

The particles are urged from the high-pressure area at the periphery of the chamber to the lower pressure zone at the centre, and enter the spaces between the paddle blades. Having processed a certain distance, the airstream comes into contact with the fast on-coming paddle and is powerfully propelled towards the periphery of the mill chamber again by the centrifugal energy imparted. The airborne material entering the space between the paddles adjacent to the leading surface and emerging along the trailing surface, therefore must cross its own path, and it is at this point of intersection that disintegration takes place. This effect is repeated as the material, under pressure from the blower and impelled by the paddles, spirals up the chamber until it is ejected by an expeller fan.

Pin Disc Mills

The Contraplex wide-chamber grinder made by Lavino (London) Ltd. can be used with nearly all soft to medium-hard materials. It is a pin disc mill in which both discs rotate at relative speeds of up to 690 ft./sec. The speed and direction of rotation of each disc are variable to suit the material being handled.

The Mikroplex spiral air classifier, supplied by this firm, is designed to allow material above a certain particle size to be repassed through the mill, and separates a fine mixture into two sharply divided fractions above and below a determined particle size. It is claimed that separations down to 2·5 microns can be obtained.

Kek Limited have recently developed a new series of belt-driven pin disc grinding mills. The first driven machine manufactured by the company, the Minikek mill, has been available to industry for the past three years. However, improvements in design have been made to enable higher rates of throughput and products of smaller particle size to be obtained from this machine. These modifications have entailed increasing the rotor speed from 15,000 r.p.m. to 19,000 r.p.m. and the horse-power of the driving motor from 1 h.p. to 1·5 h.p. in certain cases. Under these conditions products having a top size of 20 microns, and rates of throughput of 100 kg/h., are being obtained from machines operating on a continuous basis.

Features include easy cleaning, low operating temperature and simplicity of construction. The range of pin disc mills is completed by the No. 4B2 mill (5 h.p. motor) and the No. 3B2 mill (12/15 h.p. motor), both of which are also belt driven, the No. 1 mill (30/50 h.p.) and the Superkek mill. In the case of all except the latter machine, which incorporates an air separation system, throughputs range from 20 to 100 kg/h.p./hr. All the pin disc mills operate on a similar principle, since each mill is fitted with horizontal stator and rotor discs, the diameter of which vary with the size of machine. These discs, which may be smooth faced or grooved, are fitted with concentric rings of pins of either circular or square cross-section. The material to be ground is fed to the mill through a hole in the centre of the stator disc, and is reduced by impact and attrition as it is forced centrifugally through the rings of stationary and rotating pins. The particle size of the product is adjusted by varying the rotor speed and the type of discs used.

Hammer Mills

The *Tschudi* hammer mill made by W. Gardner and Sons (Gloucester) Ltd. is designed so that the particle size of the product can be varied on the same screen perforation, while the mill is running.

Raw material is fed pneumatically to the centre of the mill through a feed spout and variable input sleeve. It then passes through the rotor on to the milling zone, in a single stream. The impact area on the zone is infinitely variable between two points allowing variation in particle size without having to change the screen.

Beaters may be changed easily without dismantling the mill, a special tool for this purpose being provided. They are reversible, providing four wearing surfaces. The screen may be changed in a few seconds. This is made in three parts so that if a burst occurs, only the damaged section needs replacing.

A special claim made for the mill is its high output per h.p. which lowers grinding costs.

Immersion Ball Mill

The Silverson Immersion Ball Mill is designed to produce finely milled suspensions of insoluble solids of the mineral type in a liquid base.

Completely untreated raw materials, it is claimed, can be converted into an elegant finished product in one operation, in one vessel and in a fraction of the time required by older processes.

The basic feature of this high-speed mill is the milling head which consists of a number of balls revolving at high speed in an enclosed track. Both the track and the balls are manufactured of a specially hardened stainless steel.

The solid and liquid ingredients of the mix are drawn into the milling head, where they are intensively milled before being expelled by centrifugal force back into the body of the mix. This ensures that the whole of the mix is kept in constant motion, with the result that the joint processes of mixing and milling take place together, and at all times a completely homogeneous texture is maintained.

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DISINFECTANTS and Disinfection

By A. H. Walters, F.I.M.L.T., M.R.S.H., M.I.Biol.

Tetrachlorosalicylanilide • Antibacterials in cosmetics • Preservative combinations • Spoilage of polish emulsions • Chlorine for control of viruses • Viruses removed by flocculation

New bacteriostat

Tetrachlorosalicylanilide (TCSA) is claimed as a promising new microbiological control agent for use in soaps and detergent products, which is effective against fungi.[1] Incorporation in toilet and scrub soaps and shampoos at 0·5% is recommended. Using a conventional agar plate method cotton containing 10 p.p.m. or more of TCSA gives inhibition zones of 10-20 mm. against *S. aureus* and *Proteus vulgaris*, but not *Esch. coli*. With nylon or wool, which has a greater affinity for TCSA than cotton, no activity can be shown against any of these three organisms by the method stated. Using sensitivity test medium (Oxo) which permits more diffusion of the bacteriostat, it is possible to demonstrate activity against *Esch. coli* on cotton and against *S. aureus* on nylon and wool.

Cotton treated with high levels of TCSA shows some fungistatic activity, and also some inhibitory action against spores of *Aspergillus niger*, *Stachybotrys atra* and *Penicillium expansum* is claimed.

Some preliminary experiments on the ability of TCSA to disinfect surfaces were encouraging. TCSA, when applied in chlorinated solvent, has no affinity for textiles; the bacteriostat may be applied, however, by a dip method to confer bacteriostatic activity to the fibres. The fluorescence of TCSA renders it convenient for detection.

It is interesting to note that the suffix "stat" and not "cide" is used by the authors of this paper. This is a wise move coming from a reputable commercial laboratory.

Antibacterials for cosmetics

For control of *Candida albicans* and *Cryptococcus neoformans* in cosmetics, interest has been centred on the alkyl parahydroxybenzoates, the hexyl and heptyl esters of which appear to be more active than caprylic acid and tetramethylthiuram disulphide.[2] For the preservation of various toilet preparations 0·2% sorbic acid is recommended, but like most other such preservatives it is inactivated by non-ionics if the critical surfactant/preservative rates is exceeded. Dodecanolpolyoxyethylene neutralises the disinfectant action of hexachloraphene against *Esch. coli* in high concentrations.

Some interesting observations have been made on the action of *Tween* 80 on certain bacterial phenomena; for instance, at *p*H 6-8 *Tween* 80 completely inhibits phage adsorption by *C. diphtheriæ*, and T.B. can use *Tween* 80 as a sole carbon source, as also can a Gram-negative coccus now named *Micrococcus tweenis*. Gram-positive bacteria appear to have more acid groups to link with cations than Gram-negative bacteria. Artificial lesions in guinea pig skin can be increased by shock, which lowers the blood bactericidal action either physically or systemically or both.

Combined effect of preservatives

In terms of inhibition of growth of micro-organisms, selectivity by certain preservatives is well known, and in some cases it has been found that antimicrobial function can sometimes be increased when two preservatives are mixed together.[3] The inhibitory effect of the following preservatives was first tested singly: sorbic, salicylic, benzoic, *o*-chlorobenzoic, *p*-chlorobenzoic and formic acids, three tests of *p*-hydroxybenzoic acid, sodium sulphite and sodium metabisulphite. The test organism was an actively growing culture of *Saccharomyces cerevisiæ* obtained from Germany, but the actual tests were done in Egypt. After seven-day incubation following exposure to each chemical separately, the minimum concentrations required to effect complete inhibition was determined. These ranged from 0·069 g./litre for *p*-chlorobenzoic acid to 3·389 g./litre for formic acid.

Results showed that combinations containing half the required concentration of salicylic acid plus any of the other preservatives proved to be more inhibiting than their components when tested singly. Other combinations had a merely additive or even a less inhibiting action than their components.

Bacteria control of floor polishes

In the early days of latex paint, one manufacturer found that several cans developed a hydrocarbon type gas which caused positive pressure and bursting at the seams.[4] In another instance, a user of natural latex found that a strong odour developed in summer in the bulk storage tanks, accompanied by degenerative changes in the product. In the latter case, microbiological contamination was obviously suspected, but in the former there were no obvious changes in the product. In fact, bacterial growth had depolymerised the polymer (butadiene-styrene) and the butadiene actually caused the problem. Bacteria have been observed in floor polish emulsions, the most common being pseudomonads, the growth of which causes chemical attack on the ingredients giving rise to discoloration, odour, gas and slime.

Infection of processing plant can be prevented by periodic cleaning of storage and processing vessels with hot water, heavy duty detergents and hypochlorite or steam. As an alternative sanitising solution phenylmercuric acetate with caustic soda is sometimes used. Examination of all raw materials in polishes, including water, should exclude spoilage

bacteria. The addition of a preservative like phenylmercuric acetate is recommended and experiments are described showing the progressive killing action of this chemical.

Chlorine versus viruses

The effect on viruses of free chlorine in water is well known, but now work has appeared on the effect of residual combined chlorine on polio and Coxsackie viruses.[5] By combined chlorine is meant the residual left after reaction with ammonia and nitrogenous organic compounds with the resultant conversion to chloramines and chlororganic compounds. Virus strains were selected for this test on the basis of their resistance to residual chlorine. The experimental procedure was at 25°C., 300-3,000 infective doses of virus being added to solutions of residual chlorine 0·5-10 p.p.m., and 1 in 7 samples being removed at intervals into sodium thiosulphate. Plaque counts were made in bottle cultures of HeLa cells or monkey kidney cells inoculated with 0·5 ml. of neutralised suspension.

Results showed the disinfecting action of combined residual chlorine to be governed by *p*H, contact time and virus strain. At 25°C., *p* H 7, 9 p.p.m. of combined chlorine was required to inactivate polio virus in 30 min. and *pro rata*. The dose of combined chlorine recommended for disinfection of sewage did not inactivate the viruses studied.

Removal of viruses by flocculation

In the U.S., a study has been conducted to determine the efficiency of a two-stage flocculation process for removing Coxsackie and bacterial viruses and native coliform and total bacteria in raw Ohio river water at 5°C., 15°C., and 25°C., the critical time in relation to floc formation for the removal of these viruses and *E. coli* in the flocculation period, and the interfering effect of gum arabic on the removal of these viruses and native bacteria in raw river water by alum flocculation.[6]

Based on the results obtained in the first stage, removal of the Coxsackie virus by 25 p.p.m. of alum, *i.e.* 44 p.p.m. of filter alum, in raw river water having turbidity readings under 260 p.p.m. was 95 and 99% at 5°C.-15°C. and 25°C. respectively, and by 15 p.p.m. of alum, *i.e.* 26 p.p.m. of filter alum, 95·7% at 25°C. In the same samples removal of the bacteria showed insignificant differences between *E. coli* and total bacteria. It was slightly higher than Coxsackie virus removal with 25 p.p.m. and significantly lower with 15 p.p.m. of alum, with removal of the bacterial virus slightly but consistently lower than that of the Coxsackie virus.

The virus-removal efficiency of the $FeCl_3$ used in the second stage was comparable to that of alum, but its bacterial-removal efficiency was lower. These relatively poor results were attributed to poor floc formation due to inadequate turbidity. The lower bacterial removal was enhanced by the interfering effect of about 100 p.p.m. of calcium ion and over 10 p.p.m. of magnesium ion, the effect of which was exaggerated at lower temperatures.

Removal of Coxsackie virus by the two stages combined was 99·6% at 5°C. and 15°C., and 99·9% at 25°C. with 25 p.p.m. coagulant in each stage. With 15 p.p.m. coagulant, Coxsackie removal was 99·8% at 25°C. At the same time removal of native bacteria was 98-99 and 99·99% by 15 and 25 p.p.m. dosages, respectively, at 25°C., and about 99·99% by the 25 p.p.m. dosage at 5°C. and 15°C.

Removal of the Coxsackie virus was slightly higher in general than that of the bacterial virus, contrary to the findings in the preceding study made with water of known chemical content. The presence of calcium and magnesium ions in the raw water and the addition of CaO in the second stage were believed to have interfered with the formation of the coagulant-cation bacterial-virus complex.

The critical time for the formation of coagulant-micro-organism complex in relation to removal of viruses and *E. coli* by practical dosages of alum at 25°C. was confined to the first few minutes after addition of the coagulant. The removal of about 60% of the Coxsackie and bacterial virus by 360 p.p.m. of alum when the viruses were introduced 30 min. after the alum addition was attributed to the presence of a small amount of aluminium ion in combination with this large coagulant dose.

Gum arabic at a concentration of 20 p.p.m. was found to prevent completely the formation of floc and removal of Coxsackie and bacterial viruses and native bacteria in raw Ohio river water dosed with 15 p.p.m. of alum.

As a result of these observations, a number of suggestions were presented for obtaining practical maximum efficiency in removing viruses as well as bacteria and other particulate matter in water supplies by flocculation.

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PHARMACY'S PARLIAMENT

(*Continued from page* 487)

increasing number of medicinal specialities was presented by T. Heseltine (Great Britain). The report covered a wide field, and referred to the advantages and disadvantages of specialities, their influence on costs, duplication, substitution, and whether and how the growing dependence of the physician on specialities could or should be checked. Various aspects of the report were criticised by a number of speakers in the discussion. The value of the British National Formulary was admitted, but it tended to guide the prescriber after the manufacturer had shown the way. Criticism of the cost of specialities was challenged vigorously by C. Stevens (Great Britain), who claimed that medicines were prepared more economically in the factory than in the pharmacy. This was refuted by H. S. Grainger (Westminster Hospital), who pointed out that many products failed to sustain their reputation, and the numerous imitations frequently marketed suggested that trade-mark legislation was not really the answer. This influx and variety of products also raised financial problems for the retail pharmacist, particularly of profit margins. Some manufacturers considered that the pharmacist took too large a share, and in some countries that had led to difficulties and misunderstanding. Mr. R. Robinson (U.S.A.), referred to the Kefauver hearings on drug costs, and emphasised that it was more important for manufacturers and pharmacists to find areas of agreement than to seek and foster differences.

Analytical Chemistry

By **William I. Stephen**, PH.D., A.R.I.C.

Detergents in sewage • Soaps and cosmetics • Essential oils • Fine chemicals • Pharmaceuticals • Vitamins • Local anæsthetics Alkaloids • Drugs

FEW of these Reports on the progress of analytical chemistry pass without some mention of the problems associated with the analysis of detergents or surfactants. These economically important chemicals, often formulated into complex mixtures, present difficulties not only to the chemist engaged in analytical control work at the factories producing these materials, but also, in the long run, to those ever-alert and tireless men who watch over the safety of our streams and rivers, and protect them from gross pollution. It is as much the responsibility of the manufacturer as of the River Board chemist to devise suitable analytical methods for the determination of detergent residues in effluent water and this present Report begins with an account of one such method.

Detergents

The water or sewage sample containing an alkylbenzenesulphonate is hydrolysed with dilute sulphuric acid, then neutralised and extracted with chloroform containing a little 1-methylheptylamine.[1] The extract is evaporated, dissolved in water and re-extracted with petroleum ether containing the amine again. The amine is then removed and a complex of the detergent with methylene blue is formed in chloroform. This is determined absorptiometrically at 650 μ, using suitable filters. Calibration curves relate the extinction to concentration of the detergent. Manoxol O.T. [di-(2-ethylhexyl) sodium-sulphosuccinate] can also be determined.

The determination of inorganic sulphate in sodium lauryl sulphate[2] is effected by precipitation of lead sulphate from an ethanolic-dilute nitric acid solution of the sample with lead nitrate solution. The precipitate is filtered off, dissolved in ammoniacal E.D.T.A. in excess, and this excess is determined by titration with standard zinc sulphate with Eriochrome black T as indicator. This method is claimed to be more precise than that of the B.P.

The identification of organic sulphates and sulphonates in detergents has been described by Jenkins and Kellenbach.[3] These substances are removed by extraction with ethanol, followed, after removal of soap or free fatty acids by acidification and extraction, by precipitation of their barium salts. These are insoluble in water and hydrocarbon solvents. The i.r. spectra of the dried salts are compared with the spectra of known compounds. As a further guide, the molecular weight of the original surfactant can be determined by ignition of the precipitated salt to barium sulphate. A paper chromatographic method has been used for the separation and identification of alkanolamines in detergent powders.[4] The method is suitable for mono-, di- and tri-ethanolamine, and other alkanolamines such as 1-aminopropan-2-ol. Alkanolamides must first be hydrolysed. R_F values for the above four compounds are given; when ninhydrin is used as reagent, as little as 0·2 μg of alkanolamine can be detected.

When surfactant mixtures are refluxed for some time with 93% phosphoric acid, hydrophobic substances are formed which can be isolated and subjected to gas-liquid vapour-phase chromatography.[5] The method depends on the isolation of a neutral oil and an acid oil fraction from the reaction mixture, and before chromatography is applied the acid fraction is esterified with methanol. Good yields of the parent compounds are obtained from aromatic sulphonates, straight-chained alkyl sulphates, fatty acid amides and esters. Dioctyl sulphosuccinate gives octyl alcohols and olefins; ethylene oxide adducts of dodecyl and tridecyl alcohols, and *tert*-dodecyl mercaptan, give olefins of the parent alcohol. The breakdown products of alkane sulphonates cannot be recovered as oils by this process. A general review of methods for the analysis of synthetic detergents has been given by Smith.[6]

Related to the analysis of detergent formulations is the analysis of fluorescent brighteners which so many commercial products now contain. American workers[7] have discussed the function of these substances and detailed a method of comparative testing by spectrophotometric means. Chemical tests are also discussed.

Soaps and cosmetics

A procedure has been described[8] for the characterisation of the carboxylic acids used in fat and soap industries. This enables a characterisation and differentiation of fatty, naphthenic and resin acids to be made. The sample is oxidised with a chromic-sulphuric acid reagent under Kuhn-Roth conditions and the volatile acids are steam distilled and determined by titration with alkali. The amount of alkali required to neutralise the acids from 1 g. of starting material is called the "Kuhn-Roth Number" and is characteristic of the type of acid.

One or two publications have appeared recently on the analysis of hair dyes. In one, the identification of hair dyes in commercial preparations is described.[9] A chromatographic procedure is used after separations to isolate the phenols, amines, and aminophenols. The dyes are identified by their R_F values, their reactions on the paper with various reagents, and by comparison with standard spots. The application of the techniques to 23 commercial samples is described. Brouwer[10] has described the identification of *p*-phenylenediamine in hair dye. The method, a sensitive and specific one, makes use of the indamine reaction, or the reaction with vanillin. A chromatographic method can also be used.

Essential oils

The determination of menthyl salicylates in lemon oil has been described by Stanley.[11] These substances when added to artificial lemon oil make it spectrally indistinguishable from genuine lemon oil. Menthyl and *m*-homomenthyl salicylates both have an R_F value of 0·92 on chromatostrips by ascending development with a diethyl ether—light petroleum solvent. The coumarins and psoralens responsible for the absorption of lemon oil at 315 mμ

have R_F values below 0·50. The procedure enables the menthyl salicylates to be separated and determined spectrophotometrically on the eluate of the chromatospots at 307 mμ.

Fine chemicals

A sensitive method for the determination of sorbic acid involves heating the sample with acid dichromate and then reacting the products with thiobarbituric acid in aqueous solution.[12] The extinction of the resulting coloured solution is measured at 532 mμ Beer's law is valid over the range 1–20 μg of sorbic acid per ml.

A chromatographic technique for the quantitative determination of traces of polyhydric phenols has been developed.[13] The developing reagent is 2 : 6-dichloro-*p*-benzoquinone-4-chlorimine. The colours and R_F values are given for 18 phenols. The separation of aceto-pyrocatechol from catechol and certain 4-substituted catechol or guaiacol-type phenols makes use of paper chromatographic and electrophoretic techniques.[14] As a result of chelate formation, phenols of the catechol type move very much more slowly than those of the guaiacol type on paper impregnated with sodium molybdate, tungstate, borate or vanadate.

Pharmaceuticals

Elvidge and Proctor[15] have described an interesting application of gas chromatography in which the water content of various pharmaceutical preparations is determined. Standard solutions of water (0·5–2·0%) and 2% of *n*-pentanol are prepared in acetone; samples of the preparations are vigorously shaken with acetone with the addition of acetone and 2% *n*-pentanol. The acetonic solutions are then subjected to chromatography. The use of *n*-pentanol as an internal standard avoids the difficulty of always taking exactly the same volume of sample.

A potentiometric method has been developed for the determination of phenacetin.[16] After an acid hydrolysis, the solution is titrated with sodium nitrite using platinum and calomel electrodes. The results are quantitative and the method is unaffected by caffeine, aspirin, salicylic acid, codeine, amphetamine, amylobarbitone, and many common excipients. The determination of the constituents of A.P.C. tablets is described by Wirth.[17] The aspirin is determined by alkalimetric titration of the sample in ethanol, a correction being made for the amount of free salicylic acid present. The phenacetin is determined spectrophotometrically by hydrolysing the sample with ethanolic hydrochloric acid followed by reaction with chromic acid in an ammonium citrate solution. The extinction is measured at 543 mμ. The caffeine is determined by an iodimetric method. The complete analysis takes about 1½ hr.

Amidopyrine can be determined by titration with sulphuric acid using methyl orange as indicator.[18] Several neutral substances are without effect. In alkaline solution, amidopyrine is oxidised by permanganate or vanadate to N-acetyl-N-methyl-N-dimethyloxamoylphenylhydrazine. These methods are preferred to procedures involving picric acid or complex formation. Dick,[19] however, recommends the formation of a nickel thiocyanate complex for the qualitative and quantitative analysis of amidopyrine. This complex is very stable and insoluble in water. This reaction is specific for amidopyrine in the presence of a very large variety of possible added drugs.

French workers[20] have given conditions for the non-aqueous titration of a number of pharmaceutical products and drugs.

Vitamins

A new colorimetric determination of folic acid makes use of the colour developed when a solution of the substance in nitric acid is boiled and then made alkaline with aqueous ammonia.[21] Beer's law is valid and the extinction is measured photometrically at 485 mμ using a blue filter. As little as 8 μg of folic acid per ml. can be determined. Coulometric and chlorimetric methods have also been described for the determination of folic acid.[22] In the coulometric method, electrically generated chlorine (4 moles) reacts with 1 mole of folic acid. An alternative procedure involves direct titration of the acid with chloramine T.

An improvement in the partition column method of Theivagt and Campbell[23] for the separation of A and D vitamins has been described.[24] In place of *iso*octane as the mobile phase, light petroleum (boiling range 30°–60°) is also used. Polyoxyethylene glycol on Celite 545 is used as the stationary phase. The chemical determination of vitamin D as described by Tschapke[25] involves extraction of the vitamin with ether; vitamin A and similar compounds are removed by adsorption on activated talc. The vitamin D residue is dissolved in chloroform and is treated with a fresh solution of stannous chloride in acetyl chloride. The resulting solution is examined photometrically at about 500 mμ.

Local anæsthetics

A number of official local anæsthetics have been identified and determined as tetraphenylborates.[26] The hydrochlorides of the various bases are dissolved in a citrate buffer and a solution of sodium tetraphenylboron added dropwise until present in excess. The precipitates can be filtered off, dried *in vacuo* and then titrated in acetone solution with acetous perchloric acid. The method deals with procaine, piperocaine, naepaine, tetracaine, cinchocaine, and butethamine. Electrophoresis is used to separate procaine from *p*-aminobenzoic acid.[27] Most satisfactory results are obtained when a citrate buffer is used. Detection is by means of Dragendorff's reagent or by diazotisation and coupling with 1-naphthol. A distillation procedure[28] has been recommended by Gélébart for the rapid determination of certain anæsthetics and antispasmodics which are esters of diethylaminoethanol. The distillate containing the base is collected in standard acid.

Oscillopolarography can be used for the determination of a number of natural and synthetic anæsthetics which are not normally reducible in 1N-sodium hydroxide.[29] These substances produce characteristic incisions on the oscillopolarogram which are suitable for qualitative and semi-quantitative purposes. The method has a useful application in toxicology.

Alkaloids

Voigt[30] has studied the determination of the ergot alkaloids with *p*-dimethylaminobenzaldehyde. Various forms of this reagent do not always give a quantitative colour reaction. A new preparation of the reagent specifically for ergot alkaloids is recommended.

Recent analytical studies of reserpine are mainly concerned with its u.v. fluorescence. Kahane and Kahane[31] show that the fluorescence of reserpine is accompanied by decomposition and the appearance of a yellow colour. Fresh solutions do not fluoresce, but the fluorescence develops when the solutions are exposed to u.v. light. Chloroform solutions show a maximum at 268 mμ

and a step at 295 mμ; the ratio of the extinctions at the maximum and the step is 1·83±0·05. The absorption at 268 mμ follows Beer's law. The spectrofluorimetry of reserpine and related compounds has been examined by American workers.[32] Methanolic solutions of reserpine show fluorescent emission at 360 mμ when excited by incident light of wavelength 280 mμ; this emission is directly proportional to concentration in the range 1–5 μg per ml. This is the basis of a method for the determination of reserpine in admixture with rescinnamine which shows different fluorescence and excitation spectra. The error involved is less than ±3%.

Eschle[33] has shown that, contrary to the findings of other workers, a difference exists in the spectrophotometric curves for pure nicotine, tobacco nicotine, and tobacco-smoke nicotine. Interfering substances such as pyridine probably account for the differences. The standard curve for each individual group is found to be quite reliable.

The use of silicotungstic acid for the isolation and identification of alkaloids and toxic nitrogenous bases from biological materials has been examined.[34] The various conditions for the precipitation have been established and a *p*H of 1·2–1·8 is recommended. A method using phosphomolybdic acid as precipitant for alkaloids has also been described.[35] The excess of the reagent is masked with tartrate and the content of molybdenum in the precipitate is determined photometrically after dissolution and reduction to molybdenum blue. The method is applicable to pilocarpine, caffeine, morphine and phenazone. The determination of micro amounts of tropane alkaloids in the presence of morphine uses an ion-exchange procedure.[36] The sample is dissolved in methanol and transferred to a column of Dowex-1 resin. The alkaloids in the eluate are determined by the diazotisation procedure of Nir-Grosfield and Weissenberg.[37]

Drugs

Rink and Lux[38] describe the assay of caffeine and theobromine by titration in anhydrous medium with acetous perchloric acid. Suitable indicators are Sudan IV, Nile blue A, neutral red, malachite green, crystal violet or brilliant cresyl blue. Non-aqueous titrimetry is also recommended[39] for the analytical control of meprobamate. The sample is gently boiled under reflux with concentrated hydrochloric acid and then evaporated to dryness. The residue is dissolved in glacial acetic acid, mercuric acetate is added as titrant to the crystal violet end-point. Dioxan is then added and the titration is continued with acetous perchloric acid to a bright blue end-point. Chatten and Levi[40] have described a number of reactions for the identification and differentiation of sympathomimetic amines. The substances discussed are dextroamphetamine, amphetamine, methamphetamine, and ephedrine.

Workers at the Royal Danish School of Pharmacy have developed a new means for the identification of acetarsol.[41] The substance is nitrated by boiling with 2M-nitric acid; on cooling this solution, 2-acetamido-4 : 6-dinitrophenol is obtained as a yellow crystalline product. The test is specific for acetarsol, since other arsenical drugs do not yield this compound.

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SIZE REDUCTION REVIEW

(*Continued from page* 493)

The mill may be used effectively in any normal type of mixing vat or container, but for best results a straight-sided vessel with a tapered bottom is recommended.

Being completely portable, the machine can be moved around from vessel to vessel. A movable floor stand with rise and fall mechanism can be supplied. This will both raise and lower the machine into and out of the mix and also allow it to be wheeled from one container to another.

In addition to this machine, satisfactory results are being achieved with the cutting head which is a new adaptation on the Silverson high-speed mixer emulsifier, which has been produced to reduce in particle size organic solids both of vegetable and animal origin, the fibrous nature of which renders them difficult to process by the older type mill methods. Here again the fining down is carried out in liquid suspension.

The clearance between the blades and the cutting head is so fine that in most cases ball milling can be completely obviated—*e.g.* recently a stable emulsion of human hair has been obtained using the cutting head. This cutting head can be fitted to existing Silverson high speed mixer emulsifiers in all sizes.

▶CENTRIFUGAL MIXER

The *Entoleter* centrifugal mixer made by Henry Simon Ltd. produces a thoroughly blended and uniform mixture on a variety of powders and granular products, it is claimed. The materials to be blended are fed on to a high-speed rotor and are delivered through a hopper outlet as a completely homogeneous mix, at rates of up to 250 lb./min. The machine is being used in a variety of industries to produce uniform mixtures simply and economically. When used with equipment for accurately controlling the flow and proportion of ingredients, it provides a continuous operation. It is also easily incorporated as a final mixer in an existing processing system to cut down mixing time and reduce costs.

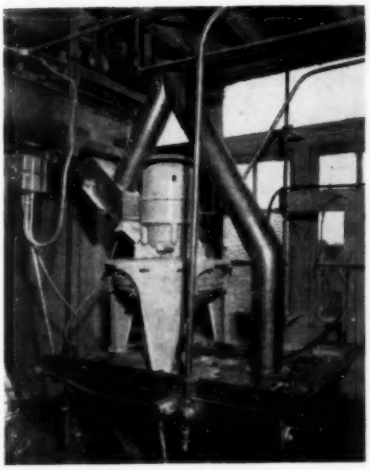
The high-speed centrifugal action breaks up and disperses small lumps of the ingredients which persist in many methods. The machine needs only 12 cu. ft. of space and, where two consecutive mixings are desirable, two machines may be mounted one above the other in less than 6 ft. of headroom.

▶EMULSIFYING AND GRINDING

Durham Raw Materials Ltd. (London, E.C.3), who last summer were appointed U.K. selling agents for Morehouse International of Los Angeles, are now able to supply a Morehouse Mill and a Cowles Dissolver on loan to firms wishing to study the productive capacity of these machines. The Cowles is a laboratory lift-up type 1-VG.

In addition, Durham Raw Materials have installed two similar machines in their laboratory at Birtley, Co. Durham, where they are at the disposal of customers seeking immediate development facilities.

The Cowles Dissolver. The important feature of the Cowles Dissolver is its patented impeller. The narrow impeller vanes, travelling at speeds up to 6,000 f.p.m., impart an extremely high velocity to the material and create a zone of intense turbulence immediately surrounding the impeller. The high velocity material impinges on the surrounding slower moving portions with "hydraulic attrition"—a combination of violent impact with the shearing of particle against particle.



The Entoleter centrifugal mixer made by Henry Simon Ltd.

This greatly multiplies the mechanical action of the impeller.

During the dispersion of solids in liquid media, hydraulic attrition breaks down the solids to ultimate dry particle size and surrounds each particle with a film of liquid. This same action is of great importance in chemical reactions to expose the greatest possible area of reactants to each other. As a dissolver, the impeller fractures friable materials, shreds soft ones and strips away softened material to expose new layers to solvent action. As an emulsifier, the impeller reduces the dispersed phase to minute particles surrounded by the continuous phase, readily and with a minimum of aeration.

Batch sizes can vary up to 6,000 gallons for the largest production models, but are dependent upon viscosity and nature of material being processed.

The Morehouse Mill. Grinding is carried out between two special grinding stones, one of which is rotated at speeds up to 9,800 f.p.m. The distance between the stones is micrometer-adjustable from positive contact to about ¼ in. in steps of 0·001 in. Adjustments can be made during operation, and the mill can be locked in position.

Highest production rates are reached at minimum temperatures, quietly and without vibration. The stones are self-sharpening. They remain true and do not glaze.

▶ROTARY TABLET MACHINE

The Manesty "B3B" machine, which replaces the B3A model, is fitted with 16 top punches, 16 bottom punches and 16 dies, mounted in a revolving turret. The material to be compressed is led from a stainless steel hopper into a special feed frame which ensures a complete and even fill of the dies, and at the same time prevents any wastage of material. At this point, the bottom punches are in their lowest position so that the dies are filled to maximum depth. As the turret revolves the bottom punches pass over a weight-adjusting cam which is set to raise the punches a definite height, which depends on the weight of the tablet being made. The excess powder is thus ejected from the dies and passed back into the feed frame. The bottom punches then drop so that the powder is not absolutely at the top of the die and this prevents any possibility of powder being ejected from the die, when the top punch enters during the compression stroke.

At compression the bottom punches pass over a pressure roller at the same time as the top punches pass under a corresponding roller. The lower pressure roller is adjustable so that the pressure under which the tablets are formed can be varied. The tablet is finally ejected and swept off the turret by the front portion of the feed frame. The adjustments for weight of the tablet and pressure can be made while the machine is running, if desired.

The turret is drilled for fitting a lower punch anti-turning device, also for the use of core rods, where required.

The "B3B" model has a redesigned weight adjusting cam which, besides being more suitable for high-speed operation, can also be removed without removing the turret.

A very important point in the operation of the new machine is that the tablets are compressed near the top of the die. The advantages of this are threefold; first it assists in preventing "capping" as the tablet is pushed only through the upper portion of the die; secondly, less pressure is required to eject the tablet and consequently wear on punches and dies is less; thirdly, the dies when worn at the top can be reversed and used again.

Addendum 1960 to the B.P. 1958

Published for the General Medical Council by the Pharmaceutical Press, London. 1960. *Pp.* 83. 30*s. net.*

THIS Addendum to the 1958 British Pharmacopœia becomes official on March 1, 1961. It contains 49 new monographs on drugs and preparations and alters some monographs in the 1958 B.P. There are also additions to and changes in the appendices of the Pharmacopœia.

Most of the new monographs are concerned with immunological products, antibiotics, or synthetic drugs. The immunological products are diphtheria and tetanus vaccine, poliomyelitis vaccine, and typhoid-paratyphoid A and B and cholera vaccine. The monographs on B.C.G. vaccine and smallpox vaccine have been revised extensively and now cover both the liquid and the dried forms.

The new antibiotic monographs deal with the calcium and sodium salts of novobiocin and the calcium and potassium salts of phenoxymethylpenicillin, and include novobiocin tablets and phenoxymethylpenicillin capsules; the monograph on phenoxymethylpenicillin tablets is revised to cover the use of the free acid and the calcium and potassium salts.

As a result of recent developments, the references to corticotrophin in the B.P. 1958 are replaced by monographs on corticotrophin, corticotrophin injection, and the long-acting preparations, corticotrophin gelatin injection and corticotrophin zinc hydroxide injection.

To the hormone preparations of the pharmacopœia are added hydrocortisone sodium succinate injection and liothyronine sodium, a salt of an active principle of the thyroid gland; the anti-thyroid substance potassium perchlorate is also introduced.

Among the new monographs on synthetic drugs are the antineoplastic agents busulphan and mercaptopurine, the antiseptics chlorhexidine hydrochloride and chlorhexidine gluconate solution, the oral hypoglycæmic agent tolbutamide, the non-mercurial diuretic chlorothiazide, the general anæsthetic halothane, and the anticholinesterase drug pyridostigmine bromide. Also included are the analeptic bemegride, phytomenadione (vitamin K_1), the renal blocking agent probenecid, and hydroxychloroquine sulphate, which is used as an antimalarial drug and for other purposes. A third piperazine salt, the citrate, and the sodium derivative of amylobarbitone are also added. There are also monographs covering the forms in which the new substances are administered. The inclusion of a monograph on tablets of phytomenadione is deferred due to the difficulty in completing the work in the time available.

The amendments made by this Addendum include changes in the requirements for tablets of dried ferrous sulphate, lucanthone hydrochloride, potassium chloride, sodium aminosalicylate, sodium chloride and sodium citrate. Among other changes are alterations in the assay of procaine penicillin, phenytoin sodium, phenytoin tablets and thyroid, and in some aspects of the monographs on neomycin, soda lime, suramin, suramin injection and suxamethonium chloride.

The table of standard preparations and units of activity of biological substances, provided in Appendix XV, has been brought up to date in accordance with the decisions of the World Health Organisation. Appendix XVIIIA, Assay of Vitamin A, is replaced by a statement that is essentially in accordance with the report of the vitamin assay subdivision of the food division of the applied chemistry section of the International Union of Pure and Applied Chemistry.

Laboratory Handbook of Toxic Agents

Editor-in-Chief Prof. C. H. Gray. Royal Institute of Chemistry. London, 1960. *Pp.* 170. 20*s. inc. postage.*

EVERYONE handling toxic materials or responsible for people handling such materials should be aware of the dangers and vigilant in using care and foresight to avoid accidents. This excellent authoritative book should accordingly have a place at the side of everyone concerned with toxic materials. It has been planned as a laboratory tool capable of giving instant advice in emergency. Three introductory chapters deal with general principles, precautions and prevention, and first aid in the laboratory. Chapter 4, the biggest, is an alphabetical list of poisonous and corrosive gases, reagents and solvents describing their hazards and appropriate first aid routines. For quick reference this section is printed on strong blue paper. Chapter 5 deals with precautions against radioactive materials and the handbook ends with a glossary of medical terms used. The book is one of a series that the Royal Institute of Chemistry intends to produce as a service to chemistry. This intention is reflected in the modest price.

Sodium Chloride

Edited by D. W. Kaufmann. Reinhold and Chapman and Hall. London. Pp. 743. 160*s. net.*

THIS book is one of the American Chemical Society Monograph series and it fully measures up to the standards of thoroughness and comprehensiveness established by that series. The editor has had 30 years' experience of the salt industry and has thus been able to utilise an expert and knowledgeable background in the compilation of the book. He has produced an encyclopædic work, but even so he claims it is no more than a selection from a vast store of information scattered through the literature. He has himself written several of the 27 chapters; the others have been contributed by experts.

The first 12 chapters deal with the occurrence of salt deposits and the various methods of processing and purification. There are three chapters on analysis and specifications. Three chapters deal with the uses of salt in physiology and nutrition—animal, human and plant. There follow chapters on materials used by the salt producing and consuming industries, and on handling and storage. Properties of salt, chemical reactions of sodium chloride and physical properties of sodium chloride are considered in chapters 23, 24 and 25. Chapter 26 deals with the economics of the salt industry on a world scale and the final chapter covers the uses of salt and brine. The book ends with a glossary of words pertaining to salt and with author and subject indexes.

This is a monumental work on a fundamental chemical raw material and it is unlikely to be challenged in its authority and scope for many years.

Chemicals and a W. European Free Market

A.B.C.M. to study effects on U.K. manufacturers

THE effects upon the chemical industry of a free market covering all Western Europe are being considered by the Association of British Chemical Manufacturers. Announcing this at the annual general meeting on October 13, the chairman of the Association, Sir Wm. Garrett, said that at the autumn meeting of presidents of European chemical associations (CEFIC) it emerged that even closer collaboration was needed to solve the difficulties arising from the separation of Europe into two economic groups.

The other important news given by the chairman was that the articles of association are being changed to permit holding companies to become members. The arrangement of having a holding company and a series of operating companies is becoming increasingly popular in industry and the Association felt it should move with the times. But the fundamental basis of membership will continue to be the manufacture of chemicals in the United Kingdom.

Annual report. As usual this ranges over a great variety of matters, from instrumentation to international trade.

Instrumentation. This committee has discovered a small initial demand for a continuous ultra-violet analyser and a meeting with potential manufacturers is being arranged. Local refresher courses for instrument mechanics are contemplated.

Dyestuffs. The repeal of the Dyestuffs Acts and their replacement by a 33⅓% duty was not welcomed by the Dyestuffs Committee. The complaint is made that the U.S. still retains a protective duty of 70-100% in spite of the concession made by Britain in surrendering the Dyestuffs Acts.

Packaging. A draft specification for paper sacks has been sent to the B.S.I. and tests are being considered.

Patents. Amendment of the Patents Act with special reference to the protection of discoveries in the agricultural field is being discussed.

Work study. A third national conference on work study is being considered.

Plant deliveries. In many cases these are still as far behind as three years ago. Stainless steel items and pumps and pump spares are most difficult. Additions to the list of standard plant and equipment issued by the B.C.P.M.A. are sought.

The A.B.C.M. Council for 1960-61 is as follows:

President: Mr. C. F. Williams (The British Drug Houses Ltd.).
Chairman: Sir William Garrett (Monsanto Chemicals Ltd.).
Vice-Chairman: Mr. J. C. Hanbury (Allen and Hanburys Ltd.).
Hon. Treasurer: Mr. J. L. Harvey (The Fullers' Earth Union Ltd.).

Anti-virus drug marketed by Winthrop

A new drug, *Virugon*, that is claimed to be effective against influenza, mumps, measles, chicken pox and shingles has been introduced by Bayer Products Ltd., one of the Winthrop group of companies. This was announced at the recent opening of the new Winthrop Group headquarters at Surbiton, Surrey, by Lord Boothby.

Virugon tablets contain N′N′ anhydrobis (β-hydroxyethyl) biguanide hydrochloride together with a small amount of scopolamine methonitrate and atropine methonitrate. The drug was discovered at the Kabi Research Institute in Sweden by a team led by Dr. B. Melander. In action it appears to interfere with the virus-host cell relationship thus stopping propagation of the virus disease.

Eleven controlled trials have shown that *Virugon* reduces the duration of influenza by one third. In prophylaxis trials the incidence of influenza has been reduced by between 50 and 80%. In chicken pox and herpes it has been found to prevent further development of the rash. The makers claim that side effects are rare and not serious.

The introduction of *Virugon* coincides with the publication of a report from the British Safety Council which states that there is a direct link between influenza and accidents. Time lost due to flu is estimated to be 20 million man-days per year and the cost £100 million. The report suggests vaccination as an answer.

Virugon retails at 18s. for 48 tablets.

Shell to spend £25m. at Carrington

The new ethylene unit at the Shell Chemical Co. works at Carrington is now on stream. Built by Kellogg International, it is designed ultimately to produce 55,000 ton p.a. from a straight run naphtha feed. In addition to high purity ethylene products, the unit produces debutanised gasoline, fuel oil, a butadiene/butylene product, with propylene and ethane, plus a refinery gas for fuel.

Other installations now in the course of construction and shown to the technical press last month include plant for the manufacture of polyethylene by both the low pressure Ziegler process and also the high pressure process. Similar plant will be installed for producing polypropylene.

A synthetic rubber plant is also proposed. Site breaking for this will commence next year and it should be operational by 1963. The design will be flexible to allow both polybutadiene and polyisoprene production. Isoprene will probably be brought from Stanlow by pipeline.

New laboratories and pilot plant buildings are now nearly completed, and will be ready in December.

The total cost of these new projects is expected to be about £25 million.

New laboratory will test additives

A D.S.I.R. grant of £22,000 p.a. for five years has been awarded to the newly formed British Industrial Biological Research Association. It will be used to help set up a biological testing station for research on the toxicity or otherwise of colours, preservatives and other chemical additives in foods, cosmetics, etc. Companies in the chemical, food and allied industries have guaranteed an income of at least £23,000 p.a. These are solid developments in what has been for many years only an idea.

A two-acre site has been obtained at Leatherhead for the laboratories. The estimated cost will be £56,000. Members of the Association's steering committee are D. W. Collier (Cadbury Bros. Ltd.); Dr. P. P. Hopf (A. Boake Roberts and Co. Ltd.); A. Norton (Rowntree and Co.); R. K. Sanders (The Metal Box Co. Ltd.); Dr. T. A. Smith (I.C.I. Ltd.); H. W. Vernon (W. J. Bush and Co.); and R. P. Woollard (London Oil Corp.).

U.S. vet drug firm buy R. F. Reed

Whitmoyer Laboratories Inc., of Myerstown, Pennsylvania, well known in North America for their veterinary products, have bought the old-established firm of manufacturing chemists, R. F. Reed Ltd., of Hertford Road, Barking, Essex. The company is now known as Whitmoyer-Reed Ltd.

It is intended to market Whitmoyer specialities in Britain as soon as possible. Meanwhile Whitmoyer-Reed will continue to make the range of pharmaceuticals and fine chemicals hitherto produced by R. F. Reed.

The new company has an American chairman, Mr. C. W. Whitmoyer, and an American managing director, Mr. G. A. Trout. Other directors are Mr. D. C. Hings and Mr. B. S. Baker.

William Freeman and Co. Ltd. have commenced production at their new Suba-Seal works at Staincross, Barnsley. A wide range of patent closures and blown polythene containers will be manufactured here.

Howards double phthalic anhydride production

Early this year, Howards of Ilford Ltd. began to make phthalic anhydride and their plant, designed to produce up to 3,000 tons/yr., is now working well. Anticipating increased demand for this product, Howards have decided to double capacity and have ordered another 3,000 ton plant. This unit will be in most respects identical with the existing unit, but will incorporate various improvements based on operational experience. It will start up in the autumn of 1961.

Howards also make phthalate esters and a big proportion of the output of the first unit goes into these, the rest being sold on the home market.

German factory for QVF

A British factory is to be built to manufacture industrial glassware, in West Germany, traditional home of glass. This new £100,000 factory, employing 50, is to be built at Wiesbaden by QVF Glastechnik, German subsidiary of QVF Ltd., manufacturers of chemical plant in glass.

Polythene tube agreement

Yorkshire Imperial Metals Ltd. and Imperial Chemical Industries Ltd. are to combine their activities in the marketing of polythene tube. Yorkshire Imperial Metals Ltd. have assumed sole responsibility for marketing Alkathene polythene tube. The combined product of the two companies will be known as Polyorc-Alkathene.

Polyorc-Alkathene is one of the few polythene tubes licensed by the B.S.I. to bear the kite mark.

Morganite Crucible Ltd.

On April 1, 1961, the crucible department will become a wholly-owned subsidiary of the Morgan Crucible Co. Ltd. It will be called Morganite Crucible Ltd. and will operate from Norton, near Worcester. The crucible sales department and some of the technical staff have been transferred from London to Norton. Any communication with the sales or technical departments at Wandsworth, London, should now be made to the Morgan Crucible Co. Ltd., Norton Works, Worcester. (Telephone: Worcester 26691.)

Mr. D. Scott will become sales director of Morganite Crucible Ltd.

"6" and "7" meeting

The presidents and directors of the Centre Européen des Fédérations de l'Industrie Chimique (CEFIC), comprising the associations of Austria, Belgium, Denmark, France, Germany, Great Britain, Holland, Italy, Sweden and Switzerland, held another meeting in October. This was one of a series at which the chemical industry has considered the economic problems of European integration and the difficulties arising from the existence of two economic groups in Europe.

Tallow manufacture

Leiner-De Mulder Ltd. has been formed by an amalgamation between a division of P. Leiner and Sons Ltd., Treforest, and a division of Prosper De Mulder Ltd. of Doncaster, where the new company will be located.

Prosper De Mulder are among the leading four renderers in Great Britain, while P. Leiner and Sons are the world's largest ossein gelatin manufacturers.

Leiner-De Mulder Ltd. will degrease animal bone and manufacture meat and bone meal and tallows.

Shell cuts resin prices

Shell Chemical Co. Ltd. have reduced the price of liquid grades of *Epikote* epoxy resins—815, 828, 834 and the solid casting resin *Epikote* 1040—by 1s./lb. on all quantities.

Borax subsidiary liquidated

As a result of internal reorganisation Joseph Townsend Ltd., an associated company in Scotland of Borax Consolidated Ltd. has ceased to trade.

A branch office of Borax Consolidated Ltd. has been established at 176, Bath Street, Glasgow, C.2 (Telephone No. Douglas 3338), with Mrs. H. McLaren as manager.

Local stocks will continue to be held in Scotland, and customers will probably find it convenient to address orders to the new Glasgow branch office rather than London head office.

Armour Hess move

The chemicals sales office of Armour Hess Chemicals Ltd. is now at 6 Arlington Street, St. James's, London, S.W.1, and all enquiries, orders, etc., concerning chemicals should be sent there. The Distec fatty acid sales office for the Greater London area will also be at that address. (Telephone: Hyde Park 7831.)

Drug research bill now over £6¼ million

The latest annual survey carried out by the Association of British Pharmaceutical Industry discloses that £6,257,025 was spent on research into and the development of new and improved drugs by A.B.P.I. members last year—an increase of more than a million pounds on 1958 and double the amount spent in 1954. The research establishments carrying out this work employed 1,374 graduates and 2,664 other staff. In addition, £273,013 was donated to independent research organisations.

Board of Trade figures show that exports of drugs have also increased. In the first eight months of this year the total exports were valued at £29·5 million as compared with £26·7 million for the comparable period of 1959 and £40·1 million for the whole year.

Announcing the research figures in the course of his presidential speech at the Association's Half-yearly Conference in Torquay, Mr. H. W. Palmer, managing director, Glaxo Laboratories Ltd., added: "All drugs placed on the market for National Health Service use are screened by an independent Health Service committee. This committee has recently undertaken to give advice and help where further clinical trials are indicated. The Association regards this as providing only a partial solution of a problem which may become acute as the industry's research efforts expand.

"The Association therefore has under consideration proposals for improving and extending the existing facilities for clinical trials in co-operation with the medical profession."

Retailers see cosmetics made

More than 80 delegates to the annual conference of the National Association of Co-operative Chemists at Bournemouth in October saw how the cosmetics they sell are made when they visited the Max Factor factory.

Later they were guests at dinner of Mr. Jack Klein, managing director of Max Factor Hollywood and London (Sales) Ltd., who received them with Mr. Sidney Factor, international director of Max Factor from Hollywood, who was on a visit to England.

Mr. Klein said: "You have seen the precise blending of our cosmetics and you will also have realised how far we have extended beyond the traditional spheres of lipsticks, skin preparations, eye make-up and the standard cosmetic range. At our factory our perfumes have their own section—in fact we have become the most important producers of quality perfume at a reasonable price. You have also seen how we are developing that important and growing market —toilet preparations for men."

A group of delegates from the annual conference of the National Association of Co-operative Superintendent Chemists watching jars of cream being boxed and packed at the Max Factor factory at Bournemouth.

Head and eye injuries in industry

The Royal Society for the Prevention of Accidents (RoSPA) has proposed two clubs, with the intention of interesting workpeople in the prevention of factory accidents. The clubs, to be known as "The Y.Z. Club" and "The Golden Eye Club," will be open to factory personnel whose foresight in wearing protective clothing designed for the purpose averted injuries to their heads and eyes while at work.

During 1959 there were 8,027 serious injuries to the head which could have been averted by helmets, and 72 fatalities caused by falling objects could have been similarly avoided. Of the 6,184 eye injuries many could have been avoided by wearing appropriate eye protection.

The Industrial Safety Division of RoSPA at 75 Victoria Street, London, S.W.1, can provide full details of membership of these clubs.

Anglo-Soviet trade in pharmaceuticals

In accordance with Article 4 of the Anglo-Soviet trade agreement of 1959, quotas have been settled for consumer goods for the year ending June 30, 1961. These quotas will be for £2·85 million worth of goods in each direction. The quota for medicines, drugs and pharmaceuticals (including raw materials) imported into this country is set at £165,000 and for export to the U.S.S.R. is £100,000.

Marchon to build detergent plants for Russia

Constructors John Brown Ltd. in association with Marchon Products Ltd., Whitehaven, have been awarded contracts by Techmashimport, Moscow, totalling nearly £3 million, for the design, supply of equipment and the commissioning of two factories to manufacture raw materials for detergents. The design of these plants will be based on Marchon experience.

WHO investigate snail killers

The WHO Expert Committee on bilharziasis is investigating new molluscicides. In many places no attempt is being made to apply the compounds which have been demonstrated as being remarkably efficient in reducing snail populations.

It is anticipated that one result of this Committee will be a report on the practical aspects of the use of molluscicides, which will be of great value to those responsible for anti-bilharziasis campaigns.

Cattle killed by arsenic

A number of cattle have been accidentally killed this year through eating potato haulm treated with arsenic. The Ministry of Agriculture has warned farmers to take special care when using arsenites. It is pointed out that by observing the precautions printed on the labelled containers both humans and animals will be safe.

Sub-sieve sizer

Kek Ltd., Manchester, United Kingdom agents for the Fisher sub-sieve sizer, now hold stocks of this equipment and it will be no longer necessary to wait for shipment from the U.S.A. Spares are also available.

Griffin and George in Manchester

The Griffin and George Group have opened their new Northern sales and service centre at Ledson Road, Wythenshawe, Manchester 23.

London warehouse for B.D.H.

British Drug Houses Ltd. are having premises in Graham Street, London, N.1, converted into a large warehouse at a cost of over £150,000.

Bush improve staff amenities

A new canteen and sports and social club has been built by W. J. Bush and Co. Ltd. at their Hackney, London, factory. The three-storey building was opened recently by Mrs. Eric Bush, the wife of the chairman. The sports and social club room is on the ground floor with facilities for dancing and games. It can hold 300 people. On the first floor, there is a billiard room and a senior staff dining room, panelled in oak. Waitress service is provided and the room can seat 60 people. On the top floor there are the two main canteens which are decorated in modern style by plastic treatment, so that the whole premises can be readily washed down and kept clean. There is also a dining room on this floor, seating 36, for the senior lady members of the staff. The modern kitchen equipment is in stainless steel and plastic and 300 meals can be prepared and served at one time. The lunches are subsidised by the company and the average price is 2s. 3d.

Company finance

Thomas Hedley and Co. Ltd. record an operating profit of £4,461,000 (£3,398,000) for the year ended June 30, 1960. Of this £2,235,000 went as tax, £1,537,000 in dividends and £689,000 is retained in the business

C. M. Fullgraf

A. Vickery

W. A. Gardiner

Charles M. Fullgraf has now taken up his appointment as managing director of Thomas Hedley and Co. Ltd. He was managing director of the toilet goods division of the Proctor and Gamble Co. (Hedley's parent company), and a member of the administrative committee in Cincinnati, Ohio. He is 42 and has two children, both at school in Newcastle.

K. W. Streith, who has been managing director since 1958, is on leave of absence on a special assignment to develop further Hedley's export business. Mr. Streith will remain a director.

Lucas Atkinson, F.C.A., and **Arthur King** have been appointed to the divisional board of Winthrop Laboratories, division of Winthrop Group Ltd. at Newcastle upon Tyne.

R. R. Feuerring, vice-president of Ferro Metal and Chemical Corp. of New York, was the chief guest at a reception in London organised by the British subsidiary, Ferro Metal and Chemical Corp. Ltd. of London, W.C.1. Mr. Feuerring, who is also a director of the British company, met several of the company's friends from Britain, France, Persia and India, together with colleagues from associated companies in Stockholm and Cologne. The organisation specialises in the supply of chemical raw materials including manganese, iron and chrome ores.

Robert B. Risk, A.M.I.CHEM.E., managing director of the Farmers' Co. Ltd., Brigg, Lincolnshire, has been elected president of the Fertiliser Manufacturers' Association, having been a member of Council since 1952. He is also a member of the committee of the Superphosphate Manufacturers' Association, of which he was chairman in 1952/3. Mr. Risk is the patentee of a process for the manufacture of "Complex" fertilisers and was a pioneer worker on the granulation of superphosphate based compounds. He lives at Barton-on-Humber with his wife and three children.

The new vice-president of the Fertiliser Manufacturers' Association is **J. S. Watkins,** M.A., B.SC. He is fertiliser products sales manager at the Billingham Division of I.C.I. He entered the fertiliser industry 27 years ago when he started at Billingham as a research chemist. He lives at Billingham with his wife and two children.

W. A. Gardiner has been appointed to the board of May and Baker Ltd. He joined the company in 1935 as a research chemist under the late Dr. A. J. Ewins. In 1942 he was appointed assistant works manager and subsequently chemical production manager. In 1955 Mr. Gardiner was appointed assistant director of production and in 1957 he joined the Board of Pharmaceutical Specialities (May and Baker) Ltd. He has been closely associated with the planning and development of the new factory at Norwich, where production commenced in 1957.

W. M. H. Stevens has been appointed deputy chairman and joint managing director of Firth Cleveland Pumps Ltd. **R. W. Hill** continues as joint managing director and will control sales activities from the Firth Cleveland group headquarters in London.

Blaw Knox Chemical Engineering Co. Ltd. have appointed **M. W. Vincent** as technical sales manager. From 1955 until 1960 he was head of the process laboratories with Sharples Centrifuges Ltd., and, before that, development chemist with Murgatroyd's Salt and Chemical Co. Ltd.

Hercules Powder Co. Ltd. London, have appointed **H. A. White** to the newly created position of assistant managing director. Mr. White, who is a Canadian, graduated from the University of Toronto as a chemical engineer and joined the paper makers chemical department of Hercules Powder Co. (Canada) Ltd. in 1947 as a technical representative.

Prof. John McMichael, F.R.S., who holds the Chair of Medicine in the University of London at the Postgraduate Medical School, Hammersmith, has been appointed a Trustee of the Wellcome Trust in place of Sir Henry Dale, O.M., F.R.S., who retired from the Trusteeship in July 1960, and was succeeded as Chairman by Lord Piercy. Sir Henry Dale will continue to serve the Trust in an advisory capacity as scientific consultant.

B. R. Hook, sales director of Price's (Bromborough) Ltd., is to leave to take up an appointment with Unilever Ltd. as marketing member of the United Kingdom chemical group. Mr. Hook, an Australian, has worked in this country since leaving Sydney University in 1946, first as a research chemist with Unilever and then in various commercial capacities.

To succeed Mr. Hook, Price's have appointed **A. Vickery.** Mr. Vickery, at present commercial sales manager, is a former research chemist. He has been a member of Price's sales management since 1956 and has played a large part in developing the company's activities in oleochemicals.

R. E. Davies, at present sales manager for the North of England, Scotland and Northern Ireland, has been appointed commercial sales manager. His colleague for the South, **T. A. Winney,** becomes home sales manager.

The Minister for Science (Lord Hailsham) has appointed **Prof. B. Bleaney,** F.R.S., and **Dr. James Cook,** F.R.S., to be members of the Council for Scientific and Industrial Research. Prof. Bleaney, who is 45, has been Professor of Experimental Philosophy at the University of Oxford since 1957. Dr. Cook, aged 59, has been Vice-Chancellor of the University of Exeter since 1955. He was President of the Royal Institute of Chemistry from 1949-51 and has been chairman of the Chemical Council since 1959. He was Regius Professor of Chemistry at the University of Glasgow from 1939-54.

Sir John Charles, chief medical officer of the Ministry of Health, the Ministry of Education and the Home Office, is retiring from the public service on November 30. He has been Chief Medical Officer since May, 1950. **G. E. Godber**, a deputy chief medical officer in the Ministry of Health, has been appointed to the joint post from December 1. After service with the London and Surrey County Councils, Dr. Godber joined the staff of the Ministry of Health as a medical officer in 1939. He was appointed senior medical officer in 1946, principal medical officer in 1948, and deputy chief medical officer in 1950.

Following the recent appointment of **A. W. Pickles,** to be accounting controller at Beecham Group headquarters, he has now relinquished the office of joint secretary of Beecham Group Ltd. **G. Hamilton,** who has hitherto held the office of a joint secretary, will continue as secretary of the company.

E. S. Sellers, who is head of the B.P. Research Centre, Sunbury on Thames, Middlesex, has accepted the invitation to be president of the Junior Institution of Engineers for 1960-61.

Prof. G. H. J. Daysh has been appointed to the board of Solway Chemicals Ltd. Prof. Daysh, who is Sub-Rector of King's College, Newcastle, holds the chair of geography in the University of Durham, and is a recognised authority on the topography and economics of Cumberland. He was closely associated with the late Lord Adams in the rehabilitation of industrial West Cumberland, and took a special interest in the development of Solway Chemicals' anhydrite mine at Whitehaven.

A. Lindsay, chief engineer of Marchon and Solway, has left Solway and is now on the board of Marchon Products Ltd. This change facilitates Mr. Lindsay's control of the Marchon engineering department in the course of the present plant expansion at Whitehaven.

Dr. A. Koebner, chief chemist of Marchon, has been appointed research director. The company's research laboratories are being enlarged and Dr. Koebner will be responsible for the whole of the research activities, which are concerned especially with detergent chemistry.

J. S. Brough has been appointed assistant managing director of Mono Pumps Ltd. Mr. Brough has held appointments as chief engineer and general manager of production at Monsanto Chemicals Ltd., and technical director of Humphreys and Glasgow Ltd.

N. J. Travis has been appointed deputy managing director of Borax Consolidated Ltd.

Union Carbide Ltd. announce the following new appointments in their sales-marketing organisation:

R. C. Agabeg, product manager, imported chemicals;
J. C. Marshall, product manager, manufactured chemicals;
R. Woollam, assistant sales manager;
R. O. Harvey, production planning co-ordinator;
J. A. Bates, Northern District manager (Manchester Office).

With the exception of Mr. Bates in the Manchester Office the other men mentioned are located at the new offices of Union Carbide at 8, Grafton Street, London, W.1. The telephone number Mayfair 8100 remains unchanged.

Macfarlan Smith Ltd., Edinburgh, announce the following appointments:

P. Mackenzie, general manager;
F. C. Griffiths, London manager at 4 Carlos Place, W.1;
G. L. Black, home sales manager;
T. N. Fraser, export sales manager;
G. Miller, company secretary.

Macfarlan Smith Ltd., which is a joint selling company formed by J. F. Macfarlan and Co. Ltd. and T. and H. Smith Ltd., has now commenced trading.

D. W. Burley, F.R.I.C., who is research manager (Administration) of Smith and Nephew Research Ltd., Hunsdon, Hertfordshire, was presented with a cheque and certificate recently to mark his 25 years' service with the Smith and Nephew group of companies. In his earlier years he was concerned with the introduction and development of surgical bandages and dressings. With the formation of Smith and Nephew Research Ltd. in 1953 he set up the technology division and more recently transferred to lead the company's administration.

The Reddish Chemical Co. Ltd., Cheadle Hulme, Cheshire, suppliers of detergents and sterilisers, have appointed **Frank Ashworth** works manager. Mr. Ashworth was previously production manager of Wm. Blythe and Co. He is 39, married, with four children.

Obituary

We regret to announce the death of **N. F. Fabricius,** an executive director of Beecham Group Ltd. As managing director and subsequently vice-chairman of County Perfumery Ltd., Mr. Fabricius was primarily responsible for the development of the Brylcreem business. In 1952 he joined the Group headquarters executive and latterly directed the Group's pharmaceutical interests as chairman of Beecham Maclean Ltd.

International Flavors and Fragrances Inc.

Since Polak and Schwarz merged with Van Ameringen-Haegler to form the new organisation International Flavors and Fragrances Inc., the Dutch branch continued to trade as Polak and Schwarz International N.V. The organisation has now decided that the time is opportune for all branches to be known as International Flavors and Fragrances. Therefore the Dutch company has been renamed International Flavors and Fragrances I.F.F. (Nederland) N.V.

Symposium on powders

The first symposium organised by the Surface Activity Group of the Society of Chemical Industry held recently at the Royal Institution, London, was attended by 411 delegates, including 31 from overseas. President of honour was Sir Alexander Fleck, who officiated at the opening ceremony.

The symposium was contributed to by 31 authors. The sections under which the papers were discussed were entitled: Principles of Production, Production, Properties of Powders, Properties of Powders Utilised in Industrial Fields, Principles of Application and Problems for the Future.

The papers presented at the symposium will be published together with the discussions, and further details can be obtained from the honorary secretary of the Surface Activity Group, Mr. M. K. Schwitzer, c/o Armour Hess Chemicals Ltd., 4 Chiswell St., London, E.C.1.

Sir Eric Rideal (left) and Mr. F. Schon, chairman of Marchon Products Ltd., at the Surface Activity Group symposium banquet.

Rubber closures for injectable products

The new British standard (BS. 3263: 1960) for vulcanised rubber closures for injectable products lays down tests and requirements which ensure that the closures form, with their appropriate seals, an effective barrier against micro-organisms after sterilisation.

The closures referred to are wads (flat rubber discs), plugs (with or without a skirt or flange) and caps (rubber covers held in position on the outside containers by the tension of the rubber).

World tour

The chairman of Laporte Industries Ltd., Mr. P. D. O'Brien, accompanied by his wife, is on a world tour. Australia is the main objective, as Laporte have a substantial business there which they want to expand. Mr. O'Brien will also visit the associated company in Bombay, National Peroxide Ltd., which also has substantial expansion plans.

Sturge to manufacture in Common Market

John and E. Sturge Ltd. have sold their citric acid manufacturing process for exploitation in the Common Market. This was one of the overseas developments foreshadowed in their prospectus in June.

A new company Biacor S.p.A. (Biochimica per la Produzione di Acidi Organici) has been formed in Italy for this purpose in which Sturge will have an important shareholding. A site has been purchased in Northern Italy providing ample space for future expansion, and planning is well advanced for the construction of the first stage of the development, with a capacity of 3,000 tons citric acid p.a. It is anticipated that production at this level will commence by the end of 1961.

Total capital required by the new company for the above stage of development is approximately £750,000.

New A.P.V. still for Grangemouth

A new general purpose batch still is to be designed and built by the A.P.V. Co. Ltd. for British Hydrocarbon Chemicals Ltd. at Grangemouth, Scotland.

The still will be used for the separation of limited amounts of intermediate and product streams into closely cut fractions. Owing to the diversity of the composition of these streams, great emphasis has been laid on flexibility and the design of distillation column adopted, which incorporates A.P.V. West plates, satisfies this requirement due to low-pressure drop and hold-up characteristics and high efficiency over a wide range of boil-up rates and reflux ratios. The unit is capable of both batch or semi-continuous operation, and of operating under vacuum.

Besides designing and building the plant, A.P.V. will also be responsible for civil and electrical engineering.

Special solvents at Kent refinery

B.P.'s first installation in the United Kingdom for the production of a range of special solvents from petroleum spirits has been commissioned at their Kent refinery. These solvents are used in the manufacture of paint and lacquers, and also in the essential oils, fatty oils and rubber industries.

One of these solvents is specially prepared and used for the unusual purpose of cleaning wigs.

The plant was designed by B.P. and has a capacity of 30,000 tons p.a. It consists of two process units for treating the oil, 17 floating roof storage tanks as well as the necessary associated pumps, piping and other facilities for handling the oil for loading road and rail tanker vehicles.

In the first process unit the petroleum feedstock is treated with strong acid in order to remove any sulphurous compounds which might give the finished solvent an objectionable odour. The second process unit then separates the spirit into the fractions required for each type of solvent. This is done within extremely stringent limits.

Mr. L. M. Spalton, chairman of the Winthrop Group Ltd., with Lord Boothby (left) who opened the new Winthrop headquarters at Surbiton.
(See p. 501)

I.C.I./Syntex agreement

I.C.I. have entered into a joint arrangement with the Syntex Corpn. under which I.C.I. will distribute Syntex pharmaceutical products under the Syntex label throughout Great Britain and the British Commonwealth.

Syntex has a fine reputation for research work in steroid chemistry and many steroid compounds now in general medical use throughout the world have emanated from their research laboratories in Mexico.

Under this arrangement the Pharmaceuticals Division of I.C.I. is now releasing for prescription by doctors an anabolic steroid, *Anapolon*, intended to restore metabolic balance and nitrogen equilibrium. It will be packed in this country by I.C.I.

Aspro take over Graesser

Aspro-Nicholas Ltd. has acquired the whole of the ordinary share capital of Graesser Salicylates Ltd. for £200,000 cash.

Graesser Salicylates Ltd. is a private company of many years' standing in the salicylate field. It has a factory at Sandycroft, near Chester, employing about 200 people, which will remain in operation. Mr. F. R. Graesser-Thomas, who founded the firm trading originally as F. R. Graesser-Thomas and Co., will remain as chairman and Mr. N. H. Graesser as president.

Meldola Medals presented

At the Royal Institution, London, W.1, on November 9, the President of the Royal Institute of Chemistry, Mr. W. Le Q. Herbert, presented Meldola Medals for 1959 to Dr. J. I. G. Cadogan and Dr. T. C. Waddington. Then followed the Meldola Medal Lecture by Dr. Waddington, entitled, "Liquid Hydrogen Halides as Ionising Solvents."

On the invitation of the Manchester University Chemical Society, Dr. Cadogan delivered his Meldola Medal Lecture, entitled "Recent Developments in Free Radical Addition Reactions," on November 1 at the University of Manchester.

Price maintenance and the Health Service

Now that price maintenance by collective action is "as dead as the dodo" it was more than ever necessary that manufacturers should be able to enforce individual price maintenance. This was said by Mr. H. W. Palmer, managing director of Glaxo and President of the Association of British Pharmaceutical Industry at a meeting of the Proprietary Articles Trade Association. Wishing P.A.T.A. well in their fight for price maintenance, Mr. Palmer said that the protection of decent margins was essential to the maintenance of the Health Service.

"It really boils down to this," said Mr. Palmer, "so complex is the job to be done to make sure that the prescribing doctor has at his disposal, quickly, through the appropriate channels, the drug of his choice, that we cannot conceive of a decent job being done unless manufacturers, wherever they may be, are enabled to protect the margins accruing both to the retail and the wholesale trade. If, in fact, the trade is not assured in that fashion of an adequate return we do not see how the very detailed and intricate service which has now to be maintained can, in fact, be underpinned and improved."

Demand for HF acid

The use for hydrofluoric acid in the electronics industry has developed so successfully in the past 18 months that James Wilkinson and Son Ltd., Sheffield, are to increase production.

Substantial tonnages in addition will also become available when a new plant, in process of completion, comes on stream early in 1961.

Institution of Chemical Engineers

November 8. "The dynamic response of a distillation column to changes in the reflux and vapour flow rates," and "An introduction to the theoretical evaluation of the frequency response of a distillation column to a change of reflux flow rate," by R. M. Wood and W. D. Armstrong. 5.30 p.m. Geological Society, Burlington House, London, W.1.

November 16. "Electrical hazards in the chemical industry," by F. Clark. 6.30 p.m. Lecture Theatre A, Houldsworth School of Applied Science, Reservoir St., Leeds 2.

November 22. "New developments in the bulk supply of chemical reagents." 3.30 p.m. Chem. Eng. Lecture Theatre, Manchester College of Science and Technology, Jackson St., Manchester 1.

December 6. "Study on electro-precipitator performance in relation to particle size distribution, level of collection efficiency, and power input," by D. O. Heinrich. 5.30 p.m. Geological Society, Burlington House, London, W.1.

December 7. "Noise problems in a large refinery," by M. B. Shirley. 6.30 p.m. Midland Hotel, Birmingham.

December 13. "Analytical instrumentation of process gas streams," by J. C. Hawkes. 7.30 p.m. Blossoms Hotel, Chester.

Royal Institute of Chemistry

November 15. Annual General Meeting. Shell Mex House, Strand, London, W.C.2. 6 p.m.

November 18. "Gastronomic chemistry," by McM. Taylor. University Chemical Laboratory, Lensfield Road, Cambridge. 8.15 p.m.

November 23. "Nucleic acids and heredity," by J. A. V. Butler. 6.30 p.m. S.W. Essex College of Technology, Forest Road, London, E.17.

November 28. "Chemical aids to crop protection," by G. L. Baldit. N.W. Kent College of Technology, Miskin Road, Dartford. 7 p.m.

November 30. "Nitration and nitrosation; a contrast," by Sir C. K. Ingold. 6.30 p.m. Battersea College of Technology, Battersea Park Road, London, S.W.11.

December 6. "Forensic science," by F. G. Tryhorn. 7.30 p.m. University Chemical Laboratory, Lensfield Road, Cambridge.

December 8. "Aromatic fluorine compounds," by M. Stacey. 6.30 p.m. Northampton College of Advanced Technology, St. John St., London, E.C.1.

Society for Analytical Chemistry

November 10. "Analytical problems in forensic toxicology," by F. L. Cann. 6.30 p.m. College of Technology, Costa Green, Birmingham.

November 22. A.G.M. and "Atomic absorption spectroscopy." 6.30 p.m. Chemical Society, Burlington House, London, W.1.

November 23. "The changing aspects of chemical analysis," by H. N. Wilson. Newcastle.

December 2. Joint meeting with Chemical Society, S.C.I. and Royal Institute of Chemistry, addressed by the President of the Society, R. C. Chirnside. Royal College of Science and Technology, Glasgow, C.1.

December 3. "Some experiences in the estimation of metals in foodstuffs," by H. Pritchard. 2.15 p.m. City Laboratories, Mount Pleasant, Liverpool.

December 7. "The flask combustion technique," London.

December 7. "Radioactivity in relation to water supplies," by F. P. Hornby. Newport.

December 8. "Problems in the control of neomycin quality," by J. W. Lightbown, a discussion meeting. 6.30 p.m. The Feathers, Tudor Street, London, E.C.4.

Society of Instrument Technology

November 17. "Spectrophotometers," by R. A. C. Isbell. Leapark Hotel, Grangemouth. 7 p.m.

November 17. "Instrumentation in the Red-Brick Industry," by M. E. C. Stedham. University of Bristol, Dept. of Physics, Bristol 8. 7.30 p.m.

Chemical Society

November 14. "Electrophilic substitution in hetero-aromatic nitrogen compounds," by J. Ridd. 5 p.m. University Chemical Laboratory, Cambridge.

November 14. "Optical rotatory dispersion in structural organic chemistry," by W. Klyne. 4.30 p.m. University of Leicester.

November 15. "Micro-organisms at work," by A. E. James. 8 p.m. Constantine Technical College, Middlesbrough.

November 16. "Problems in the chemistry of natural products," by T. B. H. McMurray. Dept. of Chemistry, University College, Dublin. 5.30 p.m.

November 17. "Polymerisation in aromatic solvents," by G. M. Burnett. Heriot-Watt College, Edinburgh. 7.30 p.m.

November 17. "Reaction mechanisms," by E. D. Hughes. 5 p.m. Royal Technical College, Salford.

November 17. "Chemical control of plant growth," by R. L. Wain. 5.30 p.m. Dept. of Chemistry, University College, Swansea.

November 18. "Phospholipids," D. M. Brown. 5 p.m. Washington Singer Laboratories, University of Exeter.

November 18. "Some photochemical reactions," by D. H. R. Barton. Chemistry Dept., University of Glasgow. 4 p.m.

November 21. "Poly-ethers," by G. Gee. 5.30 p.m. Chemistry Dept., University College, Cathays Park, Cardiff.

November 21. "Researches on some nitro-containing carbohydrates," by M. Stacey. 8.15 p.m. Inorganic Chemistry Lecture Theatre, Oxford.

November 25. "The actinomycin group of antibiotics," by A. W. Johnson. 5.30 p.m. Chemistry Dept., King's College, Newcastle.

November 28. "The kinetics of dissociation of a diatomic gas," by H. Pritchard. 5 p.m. University Chemical Laboratory, Cambridge.

November 28. "Polonium," by K. W. Bagnall. 5 p.m. Science Laboratories, The University, Durham.

November 28. "Some adventures in heterocyclic chemistry," by A. R. Katrizky. Room F1, Manchester College of Science and Technology. 6.30 p.m.

November 29. "The catalytic deuteration of some cyclic olefins on metal films," by C. Kemball. 5 p.m. Dept. of Chemistry, The University, Nottingham.

December 1. "Modern aspects and results of sulphur chemistry," by M. Becke-Goehring. 6.30 p.m. Room F1, Manchester College of Science and Technology.

December 2. "Non-aqueous titrations," by G. F. Lewis. 7 p.m. College of Technology, Portsmouth.

December 2. "Chemicals from petroleum," by R. Holroyd. 7.45 p.m. Dept. of Chemistry, Trinity College, Dublin.

December 8. "1,3-Dipolar cycloadditions," by R. Huisgen. 4.30 p.m. Lecture Theatre, The Royal Institution, Albemarle Street, London, W.1. and *December* 9 at University Chemical Laboratory, Cambridge.

University of London

November 9, 16 *and* 23. "Vibration mills and vibration milling," by H. E. Rose. 5.30 p.m. King's College, Strand, W.C.2.

Society of Cosmetic Chemists

November 21. "What determines emulsion type?" by J. T. Davies. 7.30 p.m. R.S.A., John Adam Street, London, W.C.2.

Fertiliser Society

November 24. "Ten years' experience with heavy applications of nitrogen on grassland in the Netherlands," by H. van der Molen. 2.30 p.m. Geological Society, Burlington House, London, W.1.

Institution of Plant Engineers

December 6. "Some engineering problems with chemical plant," by J. C. Veale. 7.30 p.m. White Lion Hotel, Church Street, Peterborough.

December 7. "Treatment of industrial effluents." 7.30 p.m. Polygon Hotel, Southampton.

News from Abroad

HUNGARY

Shorter hours

Ten thousand more workers in the chemical industry in Hungary are getting their working hours reduced to 40-42 per week, making 20,000 in all since the industry began three years ago to cut hours of workers doing jobs liable to affect their health.

Sections concerned include rubber, plastics, coal processing, dyes and medicines.

Two-thirds of the time lost will be made up by improved technology and one-third by extra staff. Pay will not be affected.

AUSTRALIA

New plant substance discovered

The discovery of a plant substance, pisatim, which could revolutionise the fight against fungus diseases, was announced at the recent international symposium on the chemistry of natural products in Sydney by Dr. D. R. Perrin and Dr. W. Bottomley, officers of the Commonwealth Scientific and Industrial Research Organisation division of plant industry. This substance reacts against certain plant diseases in the same fashion as antibodies in humans.

Manufacture of emulsifiers

Reichhold Chemical Industries (Australia) Ltd. and the Hercules Powder Co. of U.S.A. have registered a £1 million company—Hercules Powder Co. (Australia) Pty. Ltd.—to produce resin-based emulsifiers. The factory will be near Melbourne.

New chemical company

Charles McDonald Pty. Ltd., Sydney pharmaceutical organisation, has joined with Mead Johnson and Co. of U.S.A. in the formation of Charles McDonald Johnson Pty. Ltd., to manufacture and sell nutritional and pharmaceutical products, concentrating on lines at present made by the parent companies. Sales will be made in Australia, New Zealand and the Far East.

Four-in-one vaccine

A vaccine to give immunity against diphtheria, polio, tetanus and whooping cough, is expected to be released in Australia shortly.

Dr. Zacharin, deputy chairman of the Australian College of General Practitioners, stated that the vaccine would give long immunity, It would also eliminate the dangerous reactions inherent in the use of antitetanus serum.

At present one vaccine, Triple Antigen, is used to give immunity against diphtheria, tetanus and whooping cough; another, Salk vaccine, is used against polio.

Glucose enquiry

The Tariff Board is inquiring whether glucose exported to Australia from the U.K. which is of a class or kind produced or manufactured in Australia, has been or is being sold to an importer at an export price which is less than its fair market value at the time of shipment, and whether, if such glucose is being sold, detriment may result to the Australian industry.

Three new vaccine projects

The government owned serum laboratories in Melbourne may soon start three new vaccine research projects. These would be to develop a purified polio vaccine, a new form of influenza vaccine and another to combat measles.

WEST GERMANY

Houdry and Huels combine

Houdry Process Corpn., Philadelphia, and Chemische Werke Huels, Marl, West Germany, are forming an equally owned company to develop, manufacture and sell each company's line of catalysts. The new firm, Katalysatorenwerke Houdry-Huels G.m.b.H., will be located in Marl.

Chemische Werke Huels is the fourth largest chemical concern in Germany. In 1959 the firm had sales of $150 million. It employs 15,000 persons at Marl. The German company is a licensee of Houdry's dehydrogenation process for producing butadiene, and has also been licensed to manufacture 3-D platinum reforming catalyst.

ISRAEL

Pharmaceutical plant

A drug plant, Plantex, is being built in Natanya and is expected to open this month. The enterprise, set up by Promotex of Geneva, which is investing I£1 million in the first stage of the project, will manufacture alkaloids, glucosides and vegetable extracts.

Plantex proposes to register a number of important patents in the field of medicinal plants and will have its own research departments which will study the possibility of growing such plants in Israel.

UNITED STATES

Hoechst take-over Lloyd's

The Cincinnati firm of Lloyd Brothers Inc. has been acquired by Farbwerke Hoechst A.G., of Frankfurt-Hoechst, the West German chemical concern. The transaction was handled by Intercontinental Chemical Corporation, Hoechst's U.S. subsidiary.

Lloyd Brothers will go on with its present production lines and also represent Hoechst's interests on the U.S. market in the pharmaceutical field. The company is one of the oldest U.S. pharmaceutical manufacturers.

Growth regulant for trees

The United States Rubber Co. has reported development of a chemical growth regulant called MH-30, which puts trees into a state of temporary dormancy. In this nongrowing state, the trees can withstand lower temperatures, and therefore it may be an aid in combating frost damage to fruit trees.

Merger proposed

A proposed merger between Minnesota Mining and Manufacturing Co. and Warner-Lambert Pharmaceutical will be a profitable move for both sides. 3M has developed some promising medical products but has little marketing experience in this field, whereas Warner-Lambert have considerable experience.

The latter company's ethical drugs include Gelusil, an antiacid for peptic ulcers; Peritrate, for angina pectoris; and Nardil, a new antidepressant. Proprietary products include Listerine, Bromo-Seltzer and Anahist products. The company also markets cosmetics and toiletries.

By using the Warner Lambert marketing organisation and research facilities 3M will be able to realise the full potential of its new medical products.

D. and O. celebrates its 162nd anniversary

Dodge and Olcott Inc., the oldest company in America specialising in the manufacturing and merchandising of essential oils, aromatic chemicals, oleoresins, seasonings, flavours and perfume bases, has celebrated its 162nd anniversary.

Production of *p*-chlorothiophenol

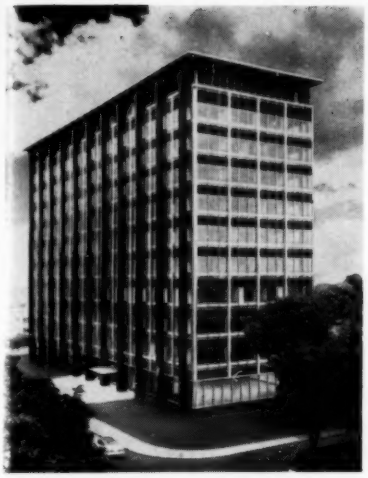
Stauffer Chemical Co. has begun commercial production of para-chlorothiophenol in Nevada, U.S.A. Hitherto the company's entire output was consumed internally.

Major potential uses are for the manufacture of oil additives, agricultural chemicals, plasticisers, rubber chemicals, dyes, wetting agents and stabilisers.

MALAYA

Arsenic weed killer banned

Sodium arsenite, widely used by big estates in the country to kill weeds and lallang, is being banned in the Federation of Malaya by the Government, following continued complaints that arsenic poisoning was causing the death of cattle. A report on the subject states that about $200,000 worth of livestock, equal to 150,000 lb. of meat, is lost annually owing to arsenic poisoning.



A new landmark in Toronto completed by Anglin-Norcross Corporation, Cubitts' Canadian associates: the eleven-storey black and silver office building for Union Carbide Canada Ltd. It cost £1,800,000 and is believed to have the largest span of any office building in the world, with interior dimensions of 210 ft. by 61 ft. It incorporates the largest amount of stainless steel curtain wall construction in Canada.

SPAIN

Dow builds petrochemical plant

An agreement has been reached between Dow and Union Quimica del Norte de Espana S.A. (Unquinesa), to construct a petrochemical complex. Unquinesa is one of the foremost Spanish manufacturers of organic and inorganic chemicals and plastics, with headquarters in Bilbao. The basis of the agreement is Dow's financial and technical participation in the development of a petrochemical industry in Spain. An approval for the joint venture already has been secured from the Spanish government.

The plan includes the construction of a cracking unit which will produce ethylene and propylene. The resulting 4C fraction will be further processed to recover butadiene. Effluent-gas will be used in Unquinesa's existing methanol plant, substituting for gasified carbon materials.

Monsanto forms new company

Monsanto Overseas S.A. has formed a new company with Aiscondel S.A. of Barcelona. The company is called Monsanto Iberica S.A.

This new venture is already in production, having acquired an Aiscondel subsidiary plant near Barcelona which produces plasticisers, stabilisers and lauroyl peroxide for the plastics processing industry.

Construction will begin immediately of a plant at Monzon to manufacture calcium carbide, acetylene and acetylene derivatives. The plant is expected to open in the second half of 1961.

SOUTH AFRICA

Alginates proposal

Alginates prepared from seaweed and used in the manufacture of ice cream and other products may be produced in South Africa if the local demand is high enough. The Fisheries Development Corporation of South Africa Ltd., a Government-sponsored concern, has asked the Cape Chamber of Industries to assist in assessing the likely demand from South African industries for alginates.

Flower preservative

Mr. P. R. Biggs, science master at the Trafalgar High School, Woodstock, Cape Town, has developed a solution which he claims doubles the life of cut carnations. In winter these carnations stay fresh in their vases for about 21 days, against the average of ten days for a cut bloom. In addition to prolonging the life of a bloom Mr. Biggs said that his formula, which is placed in a vase at a strength of three tablespoons to a pint of water, increases the size of the flower and improves its scent. His formula, which produces a transparent liquid with white flecks in it, is being kept secret until patents have been taken out. In the meantime, Mr. Biggs is experimenting with other flowers. He has found that if the concentration of the same formula is increased it prolongs the life of tulips. His formula has five main constituents and includes trace elements, mineral salts and a preservative.

MEXICO

Fluorine chemicals factory

Celulosa y Derivados S.A., Mexico, a member firm of the Monterrey Chemical Group, has approved the installation in Monterrey of factories for manufacturing hydrofluoric acid and fluorinated hydrocarbons. Their manufacture will necessitate the use of carbon tetrachloride, fluorite and sulphuric acid. The carbon tetrachloride will be manufactured in a plant belonging to the same group and now under construction in Monterrey City, and will use raw materials supplied by Quimica Industrial de Monterrey S.A. and Sosa de Mexico S.A. Quimica Industrial will manufacture the sulphuric acid required.

TECHNICAL PRESS IN NOVEMBER

The Corrosion and Metal Finishing Exhibition

Corrosion Technology devotes a considerable amount of space this month to a complete preview of the Corrosion and Metal Finishing Exhibition. New plant and new techniques to fight corrosion are all included in this very important issue.

Instrumentation for process control is featured in **Chemical and Process Engineering.** There are three articles: Process Dynamics in Process Control, Instrumentation and Control of a Pilot Plant, and Instrumentation and Control of a Distillation Plant for Chlorosilanes. Copper is reviewed in the series dealing with materials for the construction of chemical plant. Legislating for Radiation Work in Industry presents some of the safety problems that must be solved now that the use of radioisotopes is so widespread.

Fibres and Plastics reviews the latest developments in synthetic fibres. Other articles of interest are: Processing High-density Polythene, One-step Foaming of Polyethers, and Cyanoethylation of Cotton in Aqueous Medium.

The second part of Carbon Black Dispersions is published in **Paint Manufacture** and Dr. Fisk continues his series on advanced paint chemistry.

Petroleum reports on the growth of the German refining industry, one of the most important features of modern industrial Europe. The whole field of North African oil exploration is brought up to date in Petroleum Exploration in the Sahara, and the United Kingdom's own small natural gas asset is described in Reforming Natural Gas at Whitby.

Articles in **Automation Progress** include: Process Control in the Manufacture of Formica, Industrial Servo Controls, From Telemetering to Remote Automatic Control, and Practical Aids to Teaching Servo Theory.

World Crops contains three special articles on silage: New Pastures With Vast Promise, Maize for Silage in Northern Europe, and Vertical Mulching.

A report on psychrophilic bacteria in pasteurised milk is published in **Dairy Engineering,** together with Water Treatment for Steam Production and How to Tackle Effluent Disposal Problems.

This month's factory visit in **Food Manufacture** is to Lockwoods' cannery in Lincolnshire. There is also an article on stainless steels.

Specimen copies and Subscription forms are available from The Circulation Manager, Leonard Hill House, Eden Street, London, N.W.1.

THE CHEMICAL MARKET

ACETIC ACID REDUCED THIS MONTH

LONDON.—The Distillers Co. Ltd. has revised the selling price of all grades of **acetic acid.** Prices are now based exclusively on the size of the delivery and the old basis of calculating prices on contract quantities has been abolished. The revised prices give an overall reduction of about 7½% for all grades.

The price of **iodine** has risen by 2s. 4d. kg. and naturally **iodides** are up. **Zinc oxide** is also up by £2 10s. ton.

FINE CHEMICALS

Acetanilide 12½ kg. 7s. 4d. kg.
Arsenic trioxide
5 to 10-ton lots £37 ton
Ascorbic acid
100 kg. £3 6s. 6d. kg.
Aspirin
1-cwt. lots in bags 4s. 10d. „
5-cwt. 4s. 8d. „
Atropine
Sulphate, 500 g. £59 18s. 6d. kg.
Alkaloid, 500 g. £68 15s. kg.
Benzene B.P.C. 28-lb. lots 1s. 8d. lb.
Benzoic acid 12½ kg. 7s. 4d. kg.
Benzyl benzoate
1-cwt. lots 5s. lb.
Bismuth oxide B.P.C. 1934
28-lb. lots 26s. 10d. lb.
Bismuth salts 1-cwt. lots:
Carbonate 20s. lb.
Subgallate 19s. 3d. „
Salicylate 19s. 9d. „
Subnitrate 18s. „
Borax B.P.
Powder £60 10s. ton
Extra fine £61 10s. „
Boric acid B.P.
Crystal £99 „
Powder £96 10s. „
Bromine B.P.C. 7-lb. lots 6s. lb.
Caffeine 50 kg. 42s. 6d. kg.
Calamine 50 kg. 4s. kg.
Calcium gluconate
1-cwt. lots dlvd. 3s. 7d. lb.
Calcium glycerophosphate
50 kg. 28s. 6d. kg.
Calcium lactate B.P.
28-lb. lots 2s. 7d. lb.
1-cwt. lots 2s. 4d. „
Chloral hydrate 50 kg. 10s. kg.
Citric acid, B.P. Powder or granulated:
1-cwt. lots in bags 212s. cwt.
5-cwt. lots „ „ 208s. „
Codeine
Alkaloid 100 g. £138 10s. kg.
Phosphate 100 g. £110 „
Cream of tartar
1-cwt. lots £12 5s. cwt.
5-cwt. lots £12 3s. „
Ephedrine
Hydrochloride 3 kg. £7 1s. 1d. kg.
Alkaloid 3 kg. £12 7s. „
Sulphate 3 kg. £7 1s. 1d. „
Eucalyptol
1-cwt. lots 11s. lb.
5-cwt. lots 10s. 6d. „
Ferri ammonium citrate B.P.
1-cwt. lots, scales 4s. 5½d. lb.
1-cwt. lots, granules 3s. 7½d. „
Ferrous gluconate
1-cwt. lots dlvd. 6s. 3d. lb.
Gallic acid B.P.C.
1-cwt. lots 10s. „
Gluconic acid technical 50%
Minimum 12-gal. drums
19s. gal., drums extra, returnable
Glucono delta lactone
1-ton lots dlvd. 5s. net lb.
Glycerophosphoric acid
24 litres 11s. 10d. litre
Glycine (amino acetic acid)
12½ kg. 18s. 10d. kg.
Hexyl resorcinol 10 kg. £7 10s. „
Hydroquinone 12½ kg. 23s. 10d. „
Iodides
Ethyl 4 kg. bottles 62s. 9d. kg.
Mercury, red B.P.C.
12½ kg. lots 58s. 6d. „
Potassium B.P.
12½ kg. lots 19s. 10d. „
Sodium B.P.
12½ kg. lots 24s. 9d. „
Iodine, Chilean crude,
99% min. in wooden casks 17s. 4d. kg.
Iodoform
12½ kg. and under 50 kg. 42s. 6d. kg.
Lactose 50 kg. 3s. 2d. kg.
Lithium salts 5-cwt. lots
Benzoate 10s. lb.
Carbonate B.P.C. 11s. 3d. „
Chloride (commercial) powder
11s. „
„ granular 10s. 9d. „
Hydroxide 9s. 9d. „
Citrate B.P.C. 9s. „
Sulphate 8s. 6d. „
Salicylate, 10 cwt., dlvd. 9s. 9d. „
Magnesium carbonate B.P.
Light cwt. lots dlvd. £129 ton
Magnesium trisilicate 28-lb. packs
28-lb. lots 4s. 3d. lb.
1-cwt. lots 3s. 10d. „
5-cwt. lots 3s. 7d. „
Bulk rates for larger quantities are from 3s. 1d. lb. in 1-ton lots
Manganese hypophosphite B.P.C.
7-lb. lots 13s. 11d. lb.
1-cwt. lots 12s. 11d. „
Mercuric chloride B.P.
50-kg. lump 48s. 6d. kg.
Methyl salicylate 1-cwt. lots 3s. 3d. lb.
Morphine
Alkaloid, 100 g. £138 18s. 4d. kg.
Nicotinamide 1 kg. £2 10s. 6d. kg.
Nicotinic acid
12½ kg. 32s. 9d. kg
1 kg. 35s. „
Oleine, B.P. extra pale, 3/4 cwt. drums returnable carriage paid G.B.
£160 ton
Phenolphthalein 50 kg. 24s. 3d. kg.
Phosphoric acid B.P.
(s.g. 1·750) 10-carboy lots 1s. 4d. lb.
Potassium permanganate B.P.
1-cwt. lots dlvd. 1s. 11½d. lb.
Procaine hydrochloride (foreign)
2 kg. 59s. kg.
Quinine 1-oz. lots 4s. 4d. oz.
Riboflavin
100 g. 5½d. g.
10 g. 7d. „
Saccharin
500 g. £7 4s. for this quantity
Salicylic acid B.P.,
1-cwt. lots dlvd. 3s. 2½d. lb.
Silver nitrate
500 g. 5s. 1$\frac{13}{16}$d. oz.
Sodium benzoate B.P.
1-cwt. lots 2s. 9½d. lb.
1-ton lots 2s. 7½d. „
Sodium gluconate technical
3-cwt. lots dlvd. 3s. net lb.
Sodium salicylate
50 kg. 8s. 8d. kg.
12½ kg. 9s. „
Sodium thiosulphate
Crystals, photographic quality
1-ton lots 49s. cwt.
Stearic acid B.P.C. flake, carriage paid G.B. £154 ton
Strychnine 25 oz. and under.
Alkaloid 11s. 3d. oz
Hydrochloride 11s. 3d. „
Sulphate 10s. 3d. „
Sulphaguanidine
12½ kg. 33s. kg.
50 kg. 32s. „
Sulphanilamide
12½ kg. 16s. 6d. kg.
50 kg. 15s. 4d. „
Sulphathiazole 12½ kg. 39s. 9d. „
Tannic acid B.P. Levis
1-cwt. lots 10s. lb.
Tartaric acid, B.P.
Powder or granulated,
10 cwt. or more £15 cwt.
Terpineol B.P.
40-gal. drums 2s. 4½d. lb.
1-cwt. lots 2s. 7d. „
Theophylline B.P.
500 g. 27s. 6d. for this quantity
Thiamine hydrochloride
100 g. 3d. g.
1 kg. £9 5s. kg.
Thioglycollate
Ammonium 12s. 4d. to 16s. 4d. lb.
Calcium:
7-lb. lots 17s. 3d. „
5-cwt. lots 14s. 3d. „
α-Tocopherol 25-g. lots 11½d. g.
Vanillin 23s. 6d. lb.
Zinc oxide B.P.
2-ton lots dlvd. £112 10s. ton

GENERAL CHEMICALS

Acetic acid 1-ton lots dlvd. in casks/drums
80% Technical £92 ton
80% Pure £96 „
Glacial B.P. £106 „
98-100% Glacial £102 „

Acetic anhydride
1-ton lots dlvd. £128 ton

Acetone
5-gal. drums, free, non-returnable £124 ton
40 to 45-gal. drums, 10-ton lots and over £80 „

Alum, potassium granular crystals
50 kg. 1s. 2d. kg.

Aluminium hydroxide B.P.C. 34
28-lb. lots 2s. 4d. lb.

Aluminium stearate (Standard)
(Precipitate) 1-ton lots £233 10s. ton

Ammonia
Persulphate £6 13s. 6d. cwt.
Phosphate: Mono- £106 ton
Di- £97 10s. „

Amyl acetate
B.S.S. 10 tons and over £251 ton
Technical £249 „

Amyl alcohol
Technical in 1-ton lots £256 ton

Arsenic White powdered ex store £42 ton

***n*-Butyl acetate**
10-ton lots in drums £165 ton

***n*-Butyl alcohol**
10-ton lots in drums £137 10s. ton

Calcium chloride
Solid and Flake, dlvd. in 1-ton lots £16 10s. ton

Calcium oxide (Lime)
Ex marble 28-lb. lots 3s. 10d. lb.

Caustic soda
Solid in drums, dlvd. £37 16s. 6d. ton
Flake in drums, dlvd. £35 10s. 6d. ton

Chloroform B.P. ½-ton lots 2s. 11½d. lb.

Chromic acid
Dlvd. U.K. (less 2½%) 2s. 0¼d. to 2s. 0¾d. lb.

DDT (Technical) 3s. lb.

2 : 4-Dichlorophenoxyacetic acid
99% pure, 1-cwt. bags £320 ton

Dimethyl sulphate
3-cwt. drums 1s. 11d. lb.

Ether (Diethyl ether)
Tech. B.S.S. and Solvent B.P. 1-ton lots in drums 2s. lb.

Ethyl acetate
10-ton lots in drums £137 ton

Ethyl alcohol
95% Gay Lussac 66·0 o.p.
over 300,000 proof gallons per year in tank wagons
3s. 2¾d. per proof gal.

Ferrous sulphate 50 kg. 1s. 4d. kg.

Formaldehyde
40% by volume dlvd. England 1-ton lots £39 15s. ton

Glycerin
1·2627 s.g. chem. pure, 5 tons and up, 5-cwt. drums £241 10s. ton
1·2627 s.g. technical grade, 5 tons and up, 5-cwt. drums £236 10s. ton

Hexamine
1-ton lots
Technical, bulk 1s. 7¼d. lb.
B.P.C. 1s. 10¼d. lb.

Hydrochloric acid
Commercial 18s. 6d. cwt.

Hydrogen peroxide 1-cwt. lots
27·5% weight £115 ton
35% weight £138 „

Lactic acid (1-ton lots)
Pale tech. 44% by weight 1s. 3¼d. lb.
Dark tech. 44% by weight 9¼d. lb.

Magnesium chloride
Solid (ex wharf): 1-ton lots £18 10s. ton

Magnesium sulphate £15 ton

Mercurous chloride (calomel)
50 kg. 65s. kg.

Mercury sulphide, red
Ton lots and over 30s. 6d. lb.

Methylated spirits (Industrial)
Perfumery quality 500 gal. and upwards: gal.
64 o.p. 7s. 4d.
74 o.p. 7s. 11d.
5 gal.:
64 o.p. 8s. 7½d.
74 o.p. 9s. 2½d.

Methyl ethyl ketone
10 tons dlvd. in drums £134 10s. ton

Methyl isobutyl carbinol
10 tons and up, in drums, dlvd. £159 ton

Naphthalene
Crystal, dlvd., 4-ton lots, spot £66 ton
Ball and flake (ditto) £86 15s. „

Nickel sulphate
dlvd. ton lots £189 ton

Nitric acid 70% intermediate £36 ton

Pentachlorphenol
Flake, technical, in 100 lb. fibre/steel kegs dlvd. 2s. 4d. lb.

Phenol Ice crystals:
1 ton dlvd. 1s. 5d. lb.
10 tons and over dlvd. in returnable 45 gal. drums 1s. 3d. lb.

Phthalates
10-ton lots in drums
Diethyl (B.S.) £187 10s. ton
Dimethyl (B.S.) £179 ton

Potassium bromide
50 kg. 5s. 6d. kg.
12½ kg. 5s. 8d. „

Potassium carbonate
Calcined 96 to 98% (1-ton lots ex store) in bags £75 10s. ton
Hydrated (1-ton lots) £74 „

Potassium fluoride
28-lb. lots 5s. 1d. lb.

Potassium sodium tartrate
5-cwt. lots in kegs £11 cwt.

Soda ash
1-ton lots non-returnable 2 cwt. bags. from £13 15s. 6d. to £15 16s. 6d. ton

Sodium hydroxide 28-lb. lots:
sticks (1-lb. bottles) 4s. 3d. lb.
pellets „ „ 3s. 9d. „

Sodium metal 28-lb. lots 3s. 8d. „

Sodium metasilicate
Dlvd. U.K. in ton lots £26 ton

Sodium phosphate
Dlvd. ton lots: Di-sodium, crystalline £40 10s. ton
Anhydrous £88 „
Tri-sodium, crystalline £39 „
Anhydrous £86 „

Sodium silicate according to grade dlvd. in drums £12 10s. to £19 15s. ton

Sodium sulphate Ex-works:
(Glauber salt) £13 ton
(Salt cake) unground, full truck loads £8 16s. 6d. ton

Sodium sulphide
Broken, returnable drums, dlvd. ton lots £37 2s. 6d. ton
Flake, ditto £38 12s. 6d. „
Solid ditto £36 2s. 6d. „

Sodium sulphite
Commercial crystals £27 5s. ton
(Dlvd. London in 2-cwt. single non-returnable bags)

Sodium tripolyphosphate
1-ton lots £95 ton

Stannic chloride 28-lb. lots 8s. 11d. lb.

Stannous chloride 28-lb. lots 9s. 5d. lb.

Strontium carbonate
96-98% 28-lb. lots 3s. lb.

Sulphuric acid, ex-works, according to quality and quantity
B.O.V. 78% from 8s. to 10s. cwt.
C.O.V. 96% from 11s. to 14s. cwt.

Zinc chloride
28-lb. lots sticks 6s. 9d. lb.

OILS AND FATS

Palm kernel oil
Refined, deodorised, 2-ton lots, naked, ex-works £120 ton

Palm oil
Refined, deodorised, 2-ton lots, naked, ex-works £101 ton

Stearine
dlvd. free bags
Pristerene 64 flake £148 ton
Pristerene 62 flake £133 „
Pristerene 61 flake £113 „
A premium of £2 ton is charged for powder and £4 for block

GUMS AND WAXES

Agar Agar No. 1
Kobe strip 17s. lb.
Powder 21s. „

Beeswax
Dar-es-Salaam spot (nominal) £26 10s. cwt.
Sudan spot (duty paid) £24 „
Bleached white (slab) £29 10s. „
Refined yellow (slab) £26 „

Benzoin
Sumatra spot £26 10s. cwt.
Siam spot £2 5s. lb.

Candelilla Spot £23 15s. cwt.

Carnauba
Prime, Spot £38 cwt.
Fatty grey £28 „

Gum arabic Lump £9 cwt.

Karaya Powder, Spot 3s. 4d. lb.

Paraffin wax
1-ton lots, acc. to grade £105 to £130 ton

Peru balsam 10s. 3d. lb.

Shellac
No. 1 orange £14 cwt.
No. 2 orange £12 10s. „
Transparent white 4s. 3d. lb.
Pale dewaxed 6s. „

Tragacanth
No. 1 spot £152 10s. cwt.
No. 2 spot £145 „
Pale leaf £65 „
Amber £38 „
Brown to Red £29 „

NEW PATENTS

COMPLETE SPECIFICATIONS ACCEPTED

Dyestuffs

Process for the production of dyestuffs of the tetrazaporphin series. *Badische Anilin- and Soda-Fabrik A.G.* 853,364.

Isoindolone dyes and their use. *J. R. Geigy A.G.* 853,237.

Monoazo dyestuffs containing triazole rings. *Farbenfabriken Bayer A.G.* 853,013.

Process for the manufacture of metallised azo dyestuffs. *Imperial Chemical Industries Ltd.* 853,172.

Manufacture of leuco sulphuric acid esters of vat dyestuffs of the anthraquinone series. *Farbwerke Hoechst Aktiengesellschaft vorm Meister, Lucius, and Brüning.* 853,264.

Water-soluble dyestuffs containing thiocyano-triazinylamino groups. *Imperial Chemical Industries Ltd.* 852,911.

Merocyanine dye, processes of preparing it and photographic emulsions containing it. *Kodak Ltd.* 852,955.

Stabilisation of dyed polyester fibres. *General Aniline and Film Corporation.* 852,977

Azo dyestuffs of the benzineazo-pyrazolone series containing thiocyano groups. *Farbenfabriken Bayer A.G.* 852,400.

Benzine-monoazo-benzine dyestuffs. *Imperial Chemical Industries Ltd.* 852,396.

Monoazo-dyestuffs derived from cyanuric halides and their manufacture and use. *Ciba Ltd.* 852,120.

Benzine-monoazo-benzene dyestuffs. *Imperial Chemical Industries Ltd.* 852,493.

Anthraquinone dyestuffs. *Imperial Chemical Industries Ltd.* 852,604.

Miscellaneous

Production of alkyl-substituted cyclohexenones. *Distillers Co. Ltd.* 852,935.

Production of ethinyl ionol. *Badische Anilin- and Soda-Fabrik A.G.* 852,945.

Recovery of the tetrachlorides of tin, titanium and silicon. *Fabriques de Products Chimiques de Shann et de Mulhouse.* 853,115.

Method of producing allo-isocitric acid by fermentation. *Kyowa Hakko Kogyo Kabushiki Kaisha.* 852,486.

New patents are from the *Journal of Patents*, and new trade marks are from the *Trade Marks Journal*. In each case permission to publish has been given by the controller of Her Majesty's Stationery Office. Each of the publications mentioned is obtainable from the Patent Office, 26 Southampton Buildings, London, W.C.2.

NEW TRADE MARKS

APPLICATIONS

Pharmaceuticals

NEMICIDE.—801,872. *I.C.I. Ltd.*

DEFLEXOL.—804,064. *Laboratoires Millot S.A.*

DARICON. — 782,554; LUBRON. — 795,746. *Chas. Pfizer and Co. Inc.*

YORDAC.—797,210. *Dales Pharmaceuticals Ltd.*

DRAGANON.—798,098; MIROLAN.—798,107. SALVARAL.—798,112. *Roche Products Ltd.*

THOROCHEM.—799,148. *Herbert Henry Brookes.*

AERIS.—799,361. *Silten Ltd.*

BATRAMYCIN.—800,106. *Ed. Geistlich Söhne A.G.*

FURAMIDE.—800,923. *Boots Pure Drug Co. Ltd.*

EDALCAIN.—803,706. *Aktiebolaget Bofors.*

RHEUSALATE.—804,103. *Willows Francis Ltd.*

POSTULES.—804,664. *Boots Pure Drug Co. Ltd.*

HYCYN.—804,878. *Parke, Davis and Co.*

FAYDO.—805,407. *Larsons Produkte A.G.*

STREPTAIRE.—805,528. *Boots Pure Drug Co. Ltd.*

GILUCOR COMBI.—791,427. *Gebrüder Giulini G.m.b.H.*

PYRIPYRIL.—795,208. *Johann G. W. Opfermann and Sohn.*

DENCYL.—797,562. *Beecham Research Laboratories Ltd.*

TYLENOL.—799,222. *McNeil Laboratories Inc.*

SURCAPS.—801,170. *Smith Kline and French Laboratories Ltd.*

HYPACAINE.—801,547. *Calmic Ltd.*

CETRILENE.—801,906. *Wigglesworth Ltd.*

LEMSLIM.—802,896. *Thomas James Lemon.*

BEEGEEPLIN.—802,969. *British Glandular Products Ltd.*

CAPDOREL.—803,137; TALMIDOX.—803,151. *Commercial Drug and Chemical Co.*

Cosmetic and toilet preparations

JOUR DE MADAME.—800,772. *Rimmel Ltd.*

SNO-FLO.—802,658. *Cussons Sons and Co. Ltd.*

GYCLAS.—794,537. *J. R. Geigy S.A.*

Manufacturing Chemist's **ENQUIRY BUREAU**

Leonard Hill House, Eden Street, London, N.W.1.

Subscribers requiring names of suppliers of chemicals or plant should state their needs on this form, giving approximate quantities, clip it to their business noteheading and send it to the Bureau, as above. Please type or use block letters.

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For office use *No.* *Date.*

NEW COMPANIES

These particulars of new companies have been extracted from the daily register of Jordan and Sons Ltd., company registration agents, Chancery Lane, London, W.C.2.

Charles Cornforth Ltd. To take over bus. of a chemist and druggist formerly cd. on by the late Charles Cornforth at Woodfield Rd., Blackpool. £750. Dirs.: Dr. Chas. M. Cornforth and Mrs. J. P. Carter. 16.8.60. 1 Woodfield Rd., Blackpool.

Addison Chemical Ltd. 18.8.60. 36 Southampton Street, London, W.C.2. Consulting, analytical, designing and industrial chemists. £100. Dir.: Felix E. Planer.

Solihull Pharmacy Ltd. 18.8.60. 42 Bedford Avenue, London. W.C.1. £10,000. Dirs.: Norman L. Green, L. C. Icke and Alan W. Green.

John Mendus Ltd. 29.8.60. 31 Main Street, Pembroke. To take over bus. of a chemist cd. on at Pembroke by John Mendus. £2,000. Dirs.: John, Mary and Rosemary Mendus.

John Chalmers Ltd. 30.8.60. To take over bus. of chemists cd. on at 9 The Square, Wimborne, by John and Freda Chalmers. £10,000. Dirs.: J. and Freda Chalmers.

Pharmacraft Co. Laboratories Ltd. 31.8.60. 66 Queen Street, London, E.C.4. To cy. on the bus. of mnfrs. of and dlrs. in medicines, etc. £1,000. Subs.: C. W. Good and J. E. Emptage.

L. Morris (Chemists) Ltd. 1.9.60. 125 Denmark Road, Manchester 5. To take over the bus. cd. on by Louis Morris at Manchester 15. £1,000. Dirs.: L. and Hilda Morris.

Clensmaw Ltd. 1.9.60. Mnfrs. of and dlrs. in chemicals. £100. Subs.: R. J. M. Howe, 22 Chancery Lane, W.C.2, and Gertrude Wren.

Eales Chemists Ltd. 19.9.60. 147 St. George's Avenue, Sheerness, Kent. £100. Dirs.: Albert C. V. and Sophia C. Eales.

Resilex Ltd. 19.9.60. Bedford Street, Hull. Mnfrs. and dlrs. in chemicals and chemical products. £100. Subs.: W. H. Fox and E. H. Rowley.

Goodall (South Elmsall) Ltd. 20.9.60. 29 Barnsley Road, South Elmsall, nr. Pontefract. To take over bus. of chemist cd. on at South Elmsall by Wm. Goodall. £6,000. Dirs.: Wm. and Mrs. E. M. Goodall.

Comber's Pharmacy Ltd. 22.9.60. 227 Holland Park Avenue, London, W.11. £100. Dirs.: Cyril Carson and Cecilia C. J. Comber.

R. J. Brand Ltd. 26.9.60. 95 High Street, Thame. Chemists. £3,000. Dirs.: Isabel G. Brand and Rosemary I. Pudsey-Dawson.

Sixty-Five Years Ago

From MANUFACTURING CHEMIST November 1895

New Chemical Works

It is understood that the directors of the Salt Union have under their consideration the establishment of a chemical works at Weston Point, where they manufacture salt from brine, brought by a line of pipes from Northwich. Trade is so bad in Runcorn and district that it is to be hoped the Union will carry out the suggested project, and so find employment for the many chemical workers now idle.